



swissestetix

T H E B E A U T Y D O C T O R S

Montignac

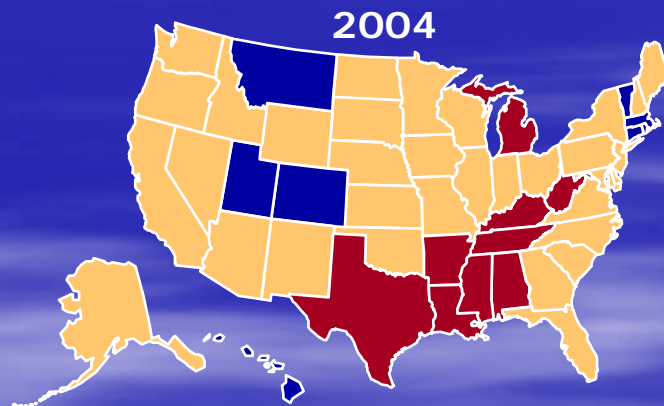
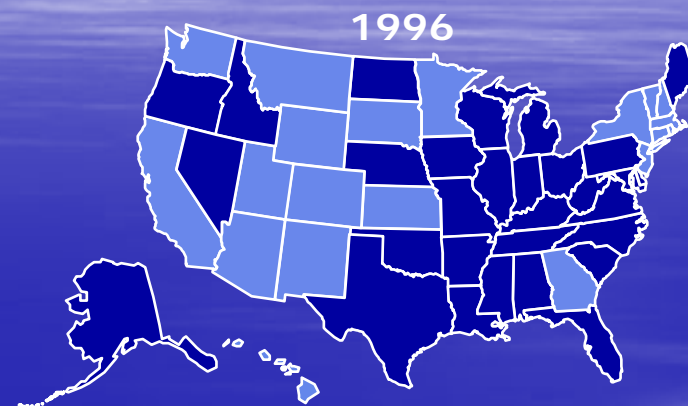
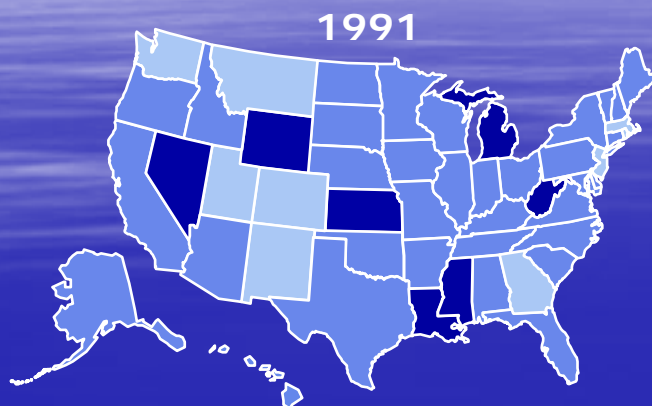
Myth or Reality?

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Obesity Trends* Among U.S. Adults

BRFSS, 1991, 1996, 2004

(BMI ≥ 30)



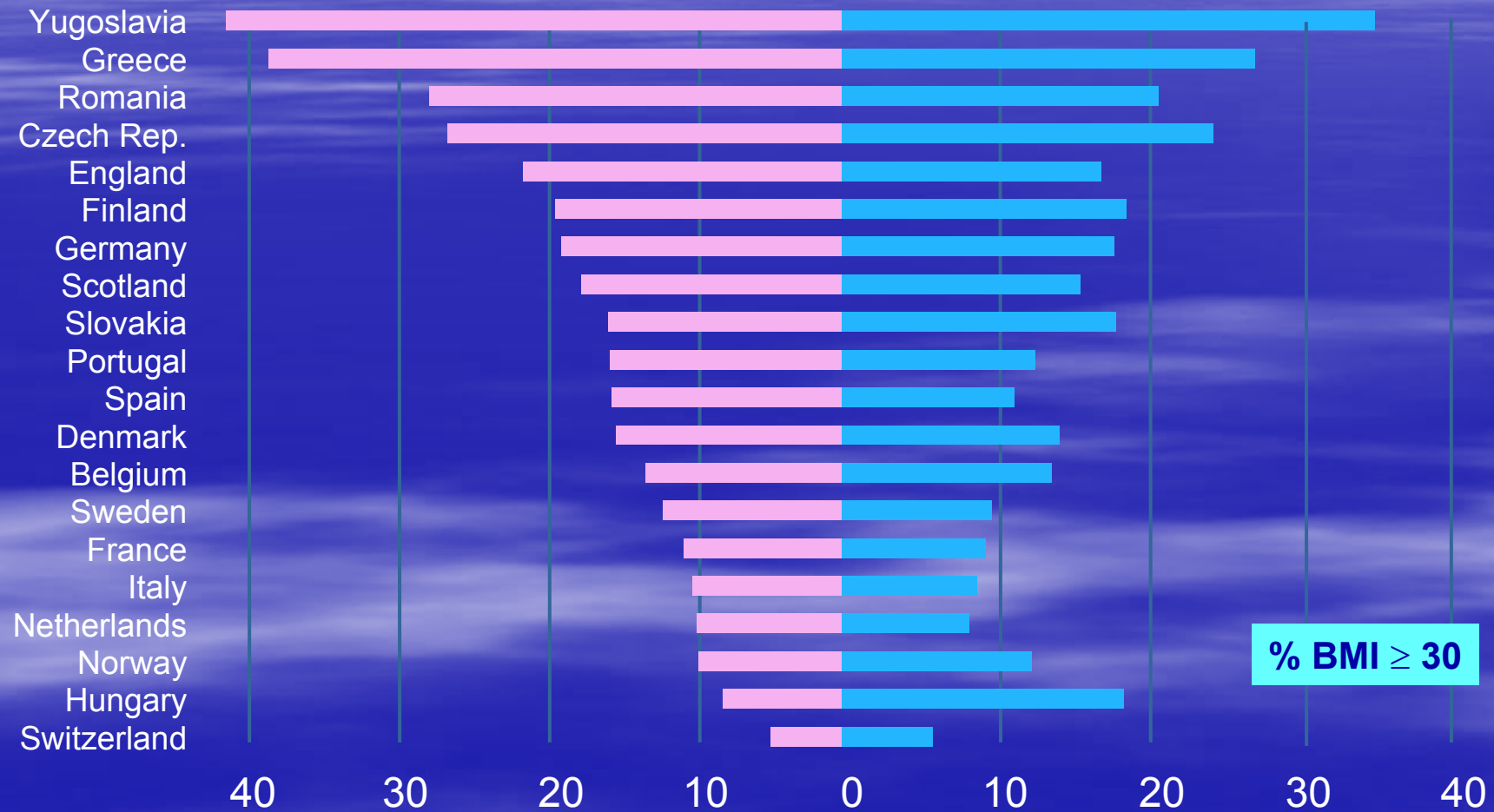
Source: Centers for Disease Control and Prevention

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Obesity in Europe

women men

Source: IOTF



The Greek Ideal

Dietary factor	Recommended dietary intake ranges (as a share of total energy intake)
Total fat	15–30%
Polyunsaturated fatty acids	6–10%
Saturated fatty acids	<10%
<i>Trans</i> fatty acids	<1%
Total carbohydrate*	55–75%
Free sugars†	<10%
Protein‡	10–15%
Cholesterol	<300 mg
Sodium chloride (sodium)	<5 g (<2 g)
Fruit and vegetables	>400 g
Total dietary fibre/non-starch polysaccharides	>25 g/20 g from whole-grain cereals, fruit and vegetables

Source: Adapted from the World Health Organization (WHO)/Food and Agriculture Organization (FAO) report *Diet, Nutrition and The Prevention of Chronic Diseases*¹, Table 6, p. 56.

*Percentage of total energy available after taking into account that consumed as protein and fat; hence the wide range.

†The term 'free sugars' refers to all monosaccharides and disaccharides added to foods by the manufacturer, cook or consumer, plus sugars naturally present in honey, syrups and fruit juices.

‡The suggested range should be seen in the light of the Joint WHO/FAO/United Nations University Expert Consultation on Protein and Amino Acid Requirements in Human Nutrition, held in Geneva, 9–16 April 2002.

Source: World Health Organization (WHO)/Food and Agriculture Organization (FAO) (2003) Diet, Nutrition and The Prevention of Chronic Diseases Report of a Joint WHO/FAO Expert Consultation. WHO Technical Report Series No. 916 Geneva WHO

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The real Picture

Nutrient/food item	Criterion	Number of countries meeting the recommendation in (3-year average):				
		1961–1963	1969–1971	1979–1981	1989–1991	1999–2001
Total protein	> 30%	0	1	1	1	1
	< 15%	0	0	0	0	0
Fat	> 30%	10	10	13	14	14
	< 15%	0	0	0	0	0
Saturated fatty acids	> 10%	9	10	11	13	12
Polyunsaturated fatty acids	< 6%	12	12	7	6	5
	> 10%	0	0	0	0	0
Carbohydrates	< 55%	8	12	13	14	14
	> 75%	0	0	0	0	0
Cholesterol	> 300 mg person ⁻¹ day ⁻¹	10	10	13	14	14
Fruits and vegetables	> 400 g person ⁻¹ day ⁻¹	6	9	9	12	14
Sugar	> 10%	8	11	10	9	10

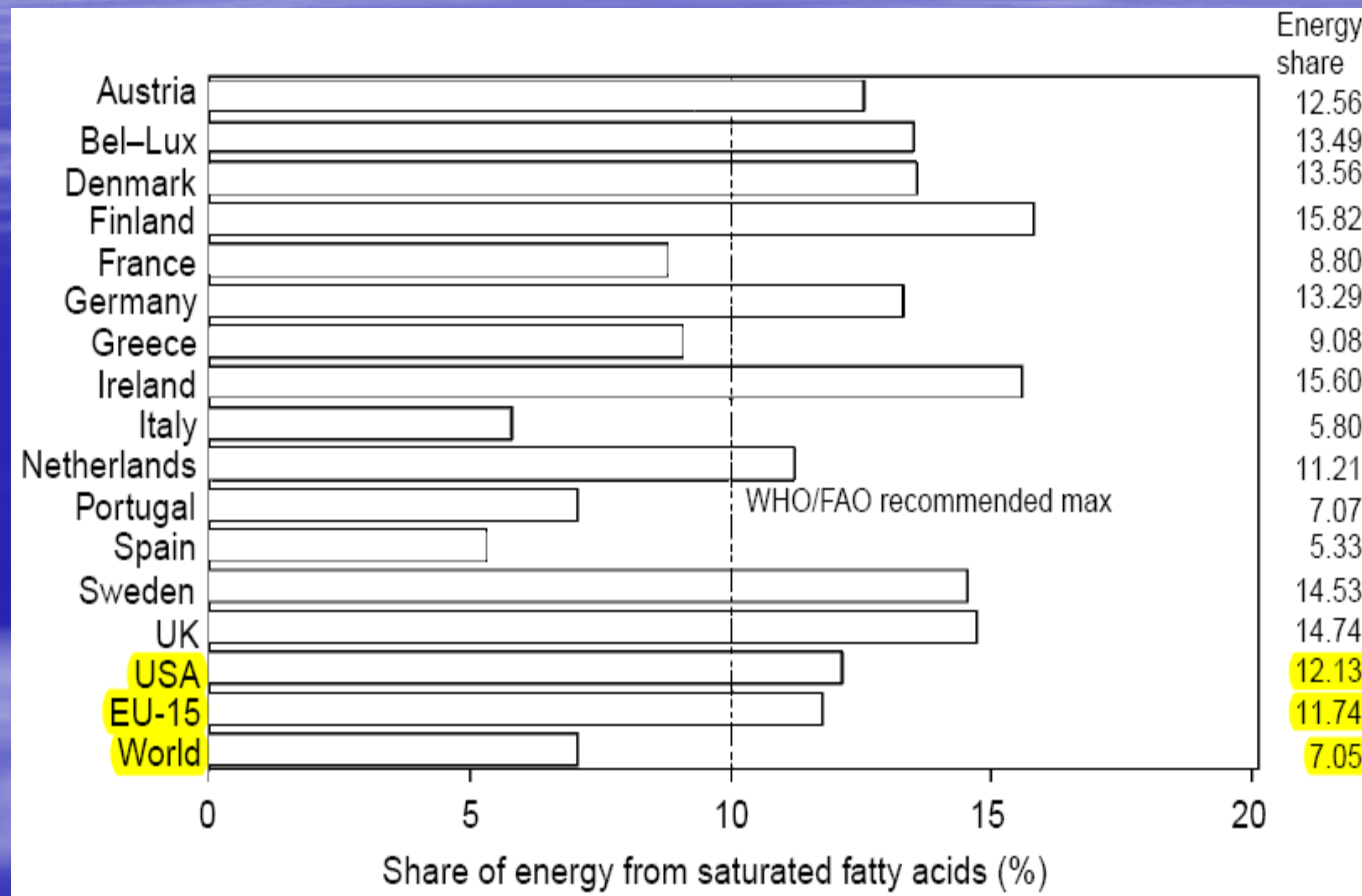
* Maximum 14.

Number of countries that meet the recommendations in the European Union.
The results of a headcount (maximum number = 14)

Source: World Health Organization (WHO)/Food and Agriculture Organization (FAO) (2003) Diet, Nutrition and The Prevention of Chronic Diseases Report of a Joint WHO/FAO Expert Consultation. WHO Technical Report Series No. 916
Geneva WHO

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The real Picture: Fat Consumption in 1961

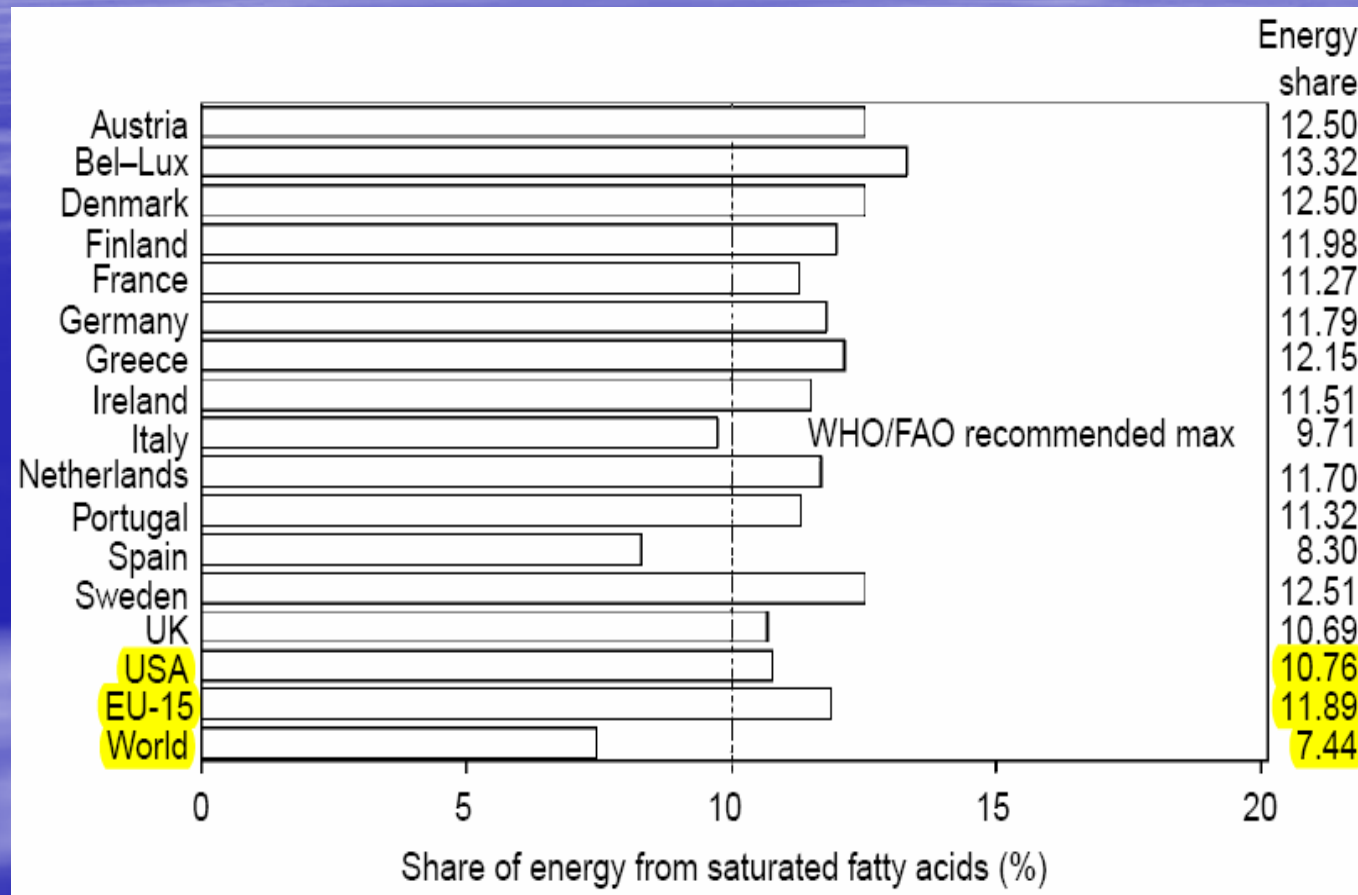


Share of energy from saturated fatty acids versus World Health Organization (WHO)/Food and Agriculture Organization (FAO) recommendation, 1961.

Source: Josef Schmidhuber, Global Perspectives Studies Group, FAO (2003)

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The real Picture: Fat Consumption in 2001

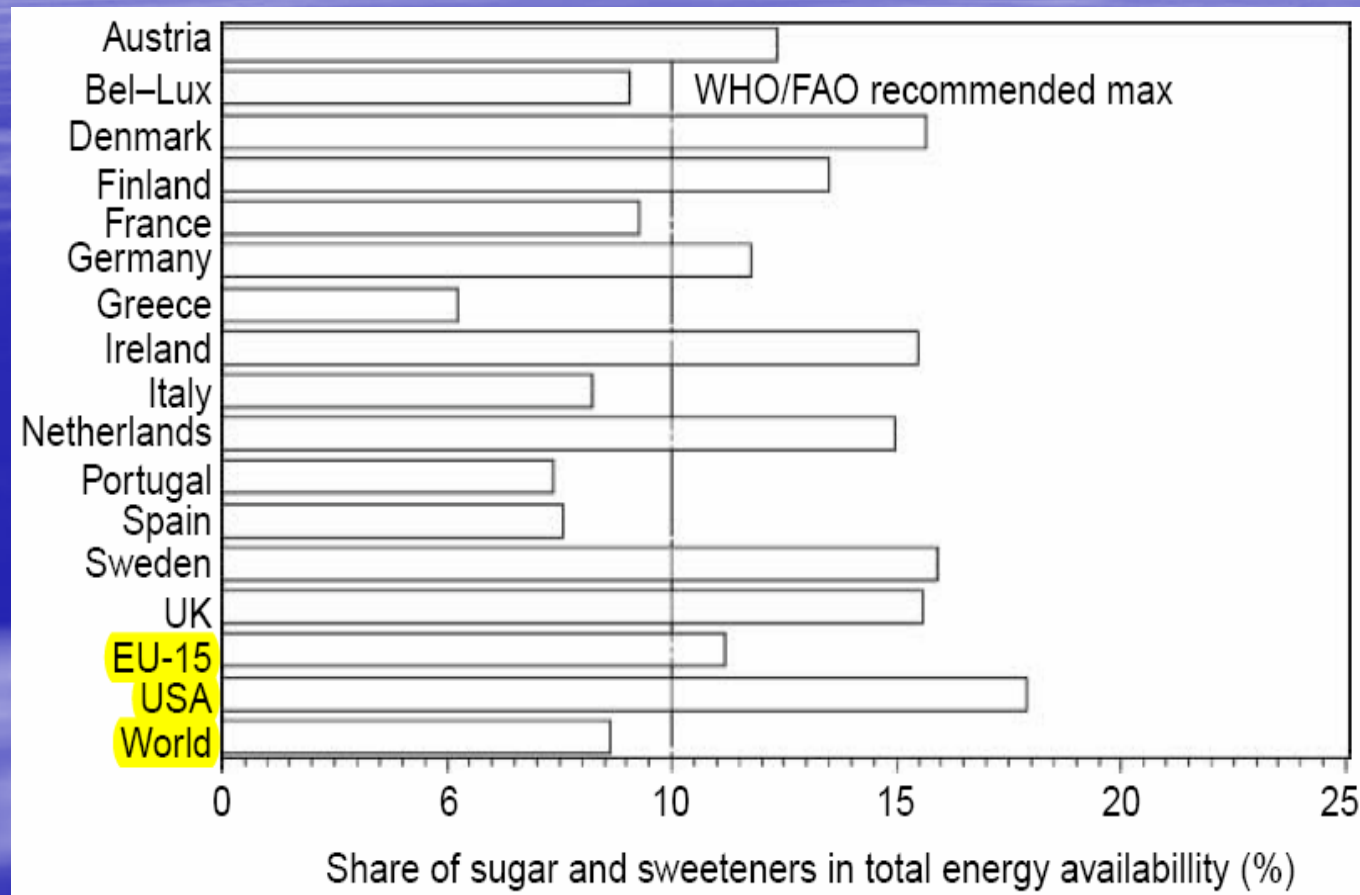


Share of energy from saturated fatty acids versus World Health Organization (WHO)/Food and Agriculture Organization (FAO) recommendation, 2001.

Source: Josef Schmidhuber, Global Perspectives Studies Group, FAO (2003)

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The real Picture: Sugar Consumption in 1961

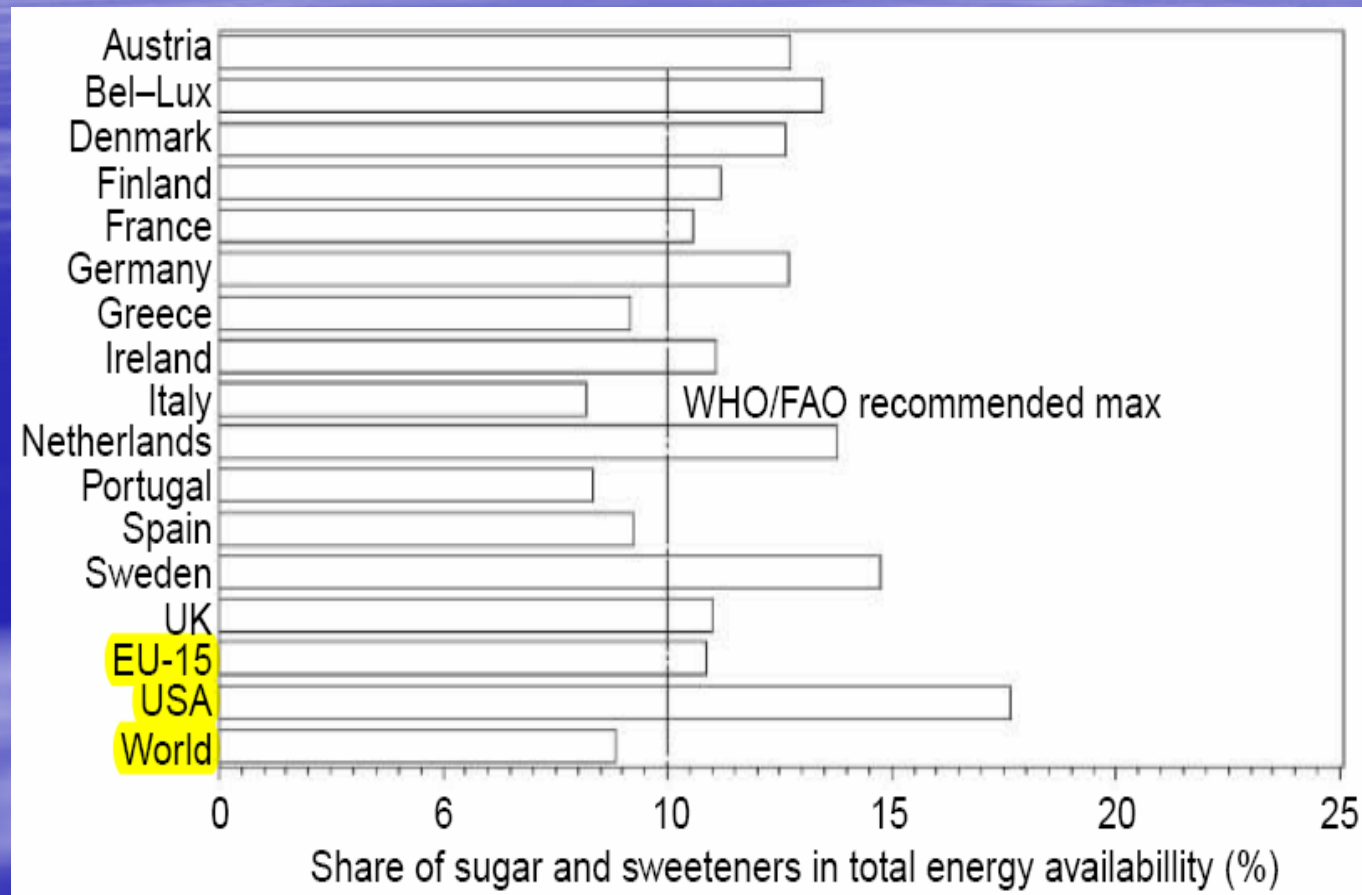


Share of energy from free sugars versus World Health Organization (WHO)/Food and Agriculture Organization (FAO) recommendations, 1961.

Source: FAO's FAOSTAT database (2003)

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The real Picture: Sugar Consumption in 2001



Share of energy from free sugars versus World Health Organization (WHO)/Food and Agriculture Organization (FAO) recommendations, 2001.

Source: FAO's FAOSTAT database (2003)

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Starting Point: The Glycemic Index Hypothesis

- “Wenn man zu Übergewicht neigt, ist dies bekanntlich darauf zurückzuführen, dass eine Funktionsstörung der Bauchspeicheldrüse vorliegt, die sich durch eine übermässige Insulinabsonderung äussert. Unsere Ernährungsstrategie besteht nun darin, die Lebensmittel mit einem hohen glykämischen Index zu meiden und die Lebensmittel zu bevorzugen, die einen niedrigen glykämischen Index aufweisen ()”.

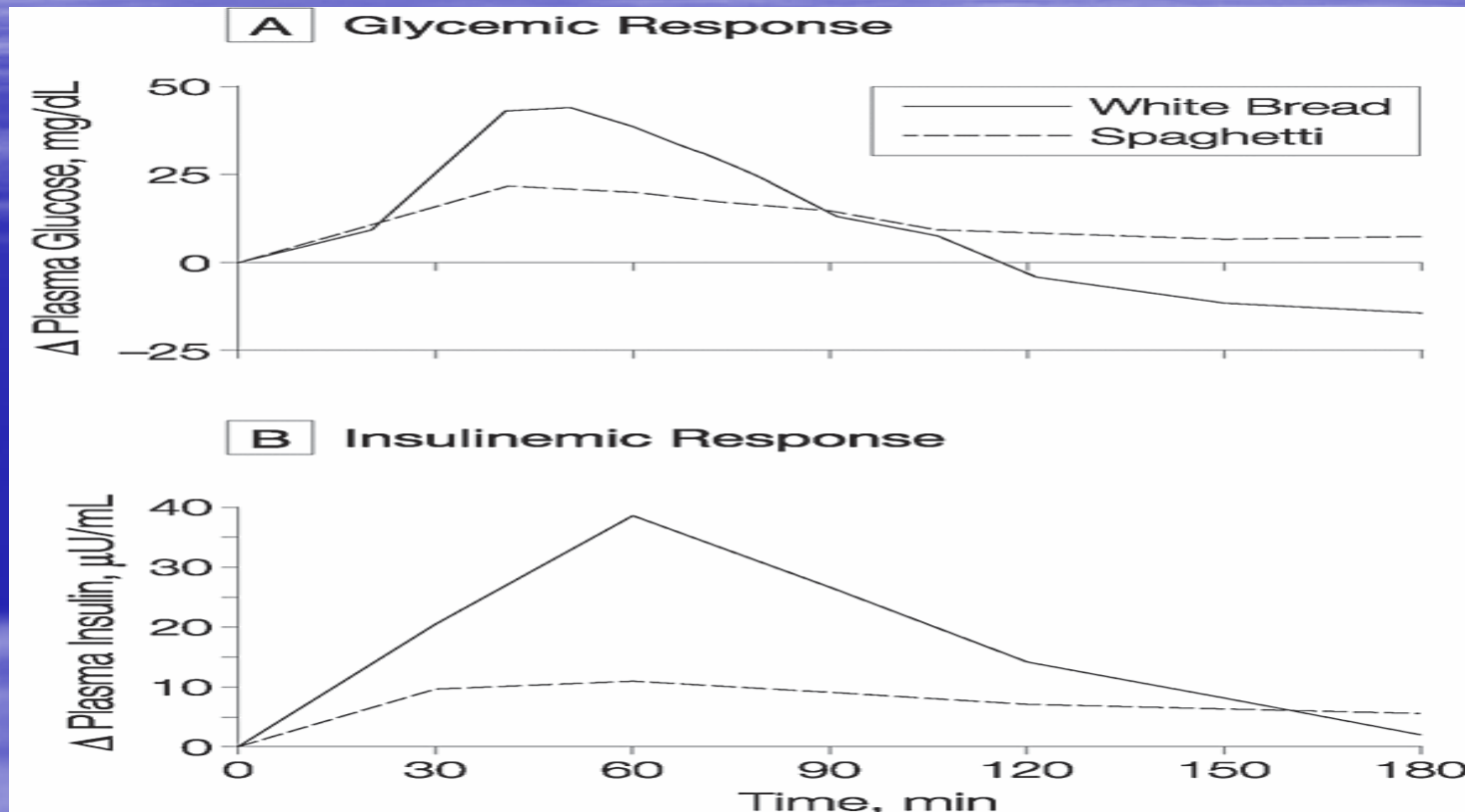
Glucose Physiology

- Obligatory requirement for glucose, approaching 200 g/d
 - Metabolic demands of the brain
- Acute hypoglycemia: blood glucose level below 2.2 mmol/l
 - Coma, seizure, death
- Acute hyperglycemia: blood glucose level above 10.0 mmol/l
 - Immediate reaction: glycosuria
 - Long term reaction: renal failure, retinopathy, atherosclerosis
- Hyperglycemia stimulates insulin secretion, promoting uptake of glucose by muscle and adipose tissue
- Hypoglycemia elicits secretion of glucagon, epinephrine, cortisol, and growth hormone antagonizing insulin action and restoring normoglycemia

Definitions: Glycemic index

- Glycemic index is defined as the incremental area under the glucose response curve for 2 hours after a standard amount (50 g) of carbohydrate from a test food relative to that of a control food (either white bread or glucose) is consumed

Glycemic and Insulinemic Responses After Ingestion of Carbohydrates



Responses were measured after ingestion of 50 g of CHD as white bread or spaghetti made from the identical ingredients

Ludwig, D. S. JAMA 2002;287:2414-2423.

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Definitions: Glycemic load

- Glycemic load is defined as the weighted average glycemic index of individual foods multiplied by the percentage of dietary energy as carbohydrate

Glycemic Index and Glycemic Load: Values of Representative Foods

Food	Glycemic Index†	Glycemic Load‡
Instant rice	91	24.8 (110 g)
Baked potato	85	20.3 (110 g)
Corn flakes	84	21.0 (225 mL)
Carrot	71	3.8 (55 g)
White bread	70	21.0 (2 slices)
Rye bread	65	19.5 (2 slices)
Muesli	56	16.8 (110 mL)
Banana	53	13.3 (170 g)
Spaghetti	41	16.4 (55 g)
Apple	36	8.1 (170 g)
Lentil beans	29	5.7 (110 mL)
Milk	27	3.2 (225 mL)
Peanuts	14	0.7 (30 g)
Broccoli

Glycemic load is calculated as the glycemic index multiplied by grams of COH per serving size, indicated in parentheses, divided by 100%.

Ludwig, D. S. JAMA 2002;287:2414-2423.

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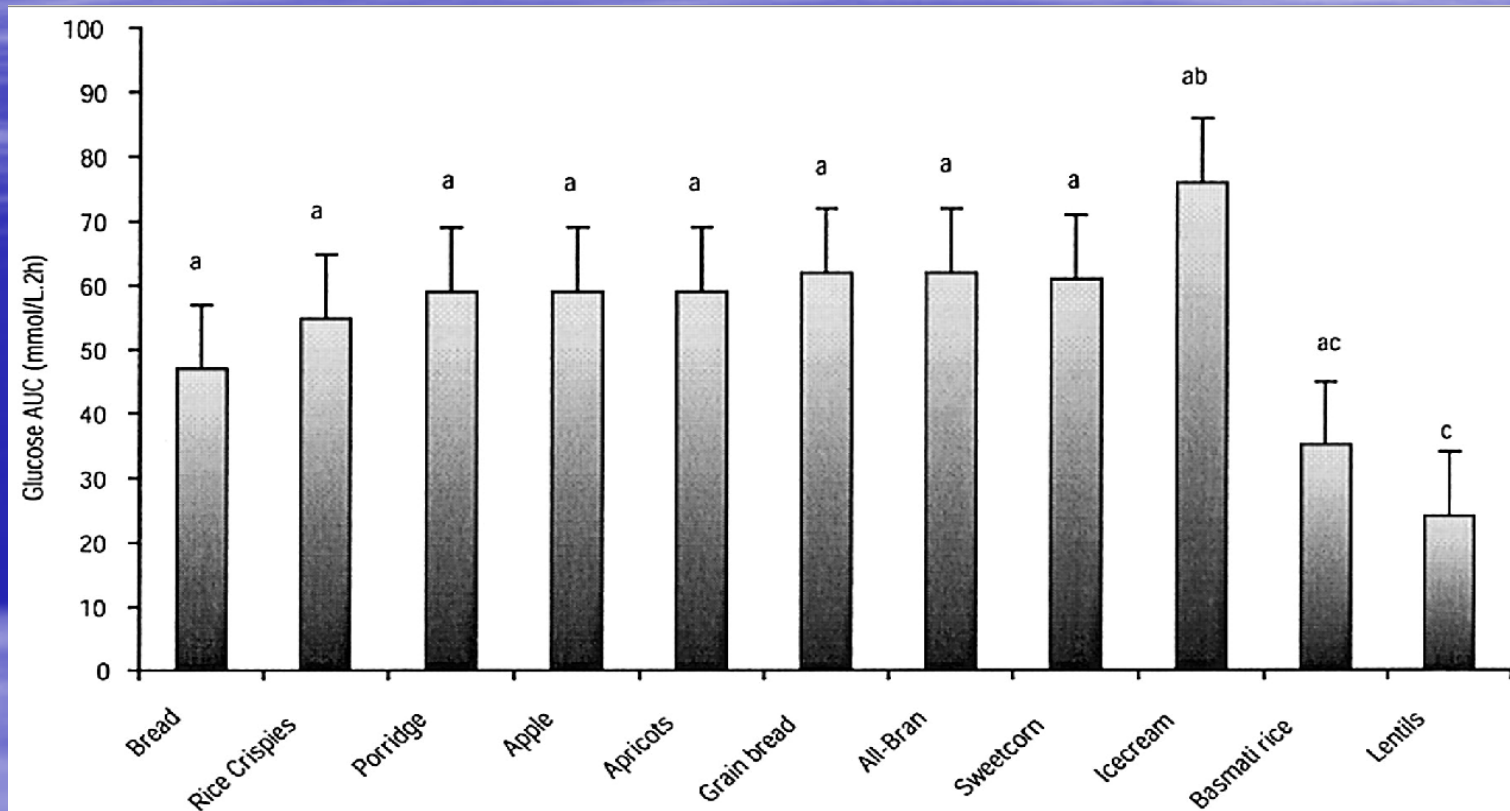
Glycemic Index and Glycemic Load: Is the Concept Valid?

The assumed glycemic index (GI) and carbohydrate (CHO) content used to calculate the weight of food portions tested in Study 1¹

Food	GI (glucose = 100)	CHO g/100 g	CHO content of portion tested g	Weight of portion tested
White bread ²	70	44	15	34
Porridge ³	41	61	25	41
Dried apricots	31	48	34	76
Apple ⁴	36	12	30	247
Grain bread ⁵	31	29	34	118
Ice cream ⁶	50	31	21	68
Lentils ⁷	26	29	40	138
Sweet corn ⁸	55	19	19	100
All-Bran ⁹	42	45	26	58
Rice Bubbles ¹⁰	81	87	13	15
Basmati rice ¹¹	58	64	18	28

All portions had the same dietary glycemic load as one slice of white bread.

Glycemic Index and Glycemic Load: Is the Concept Valid?

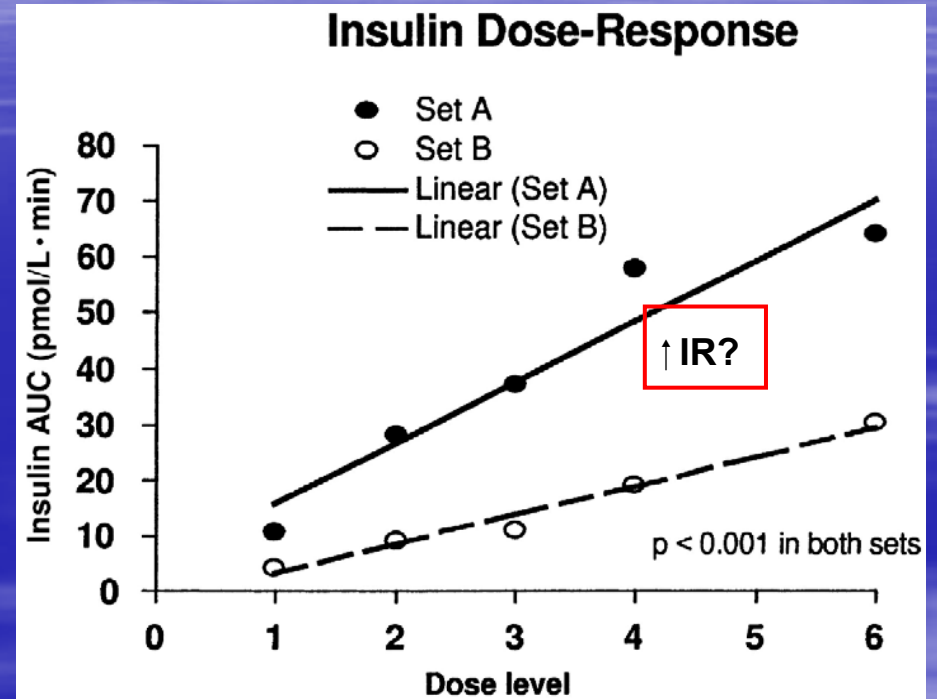
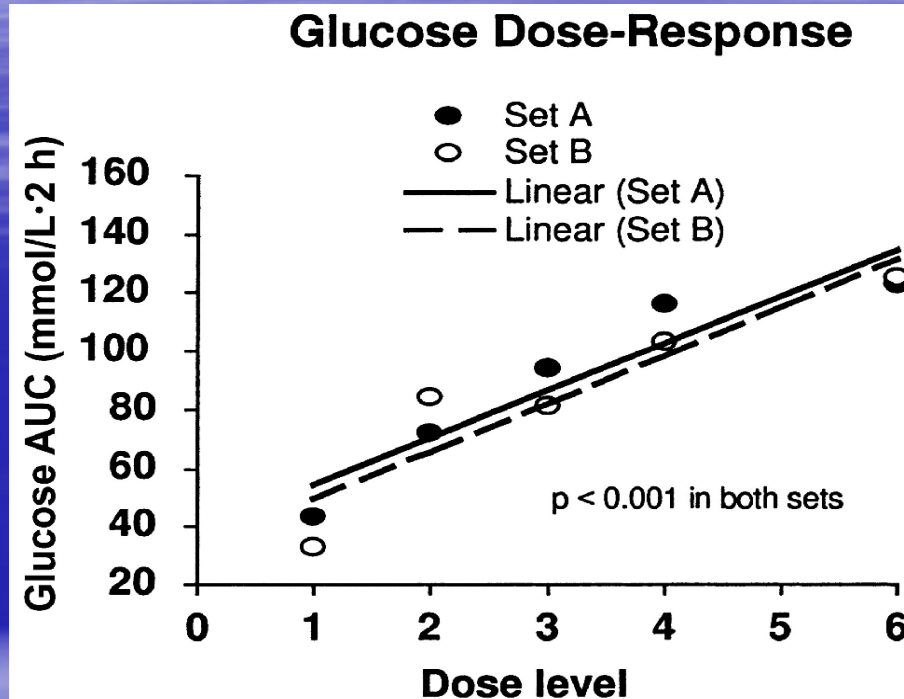


Human subjects received 10 different foods in portion sizes calculated to be equivalent in dietary glycemic load to one slice of white bread. Values are mean $AUC \pm SEM$, $n=10$, for each food.

Brand-Miller JC et al J Nutr. 2003 Sep;133(9):2728-32

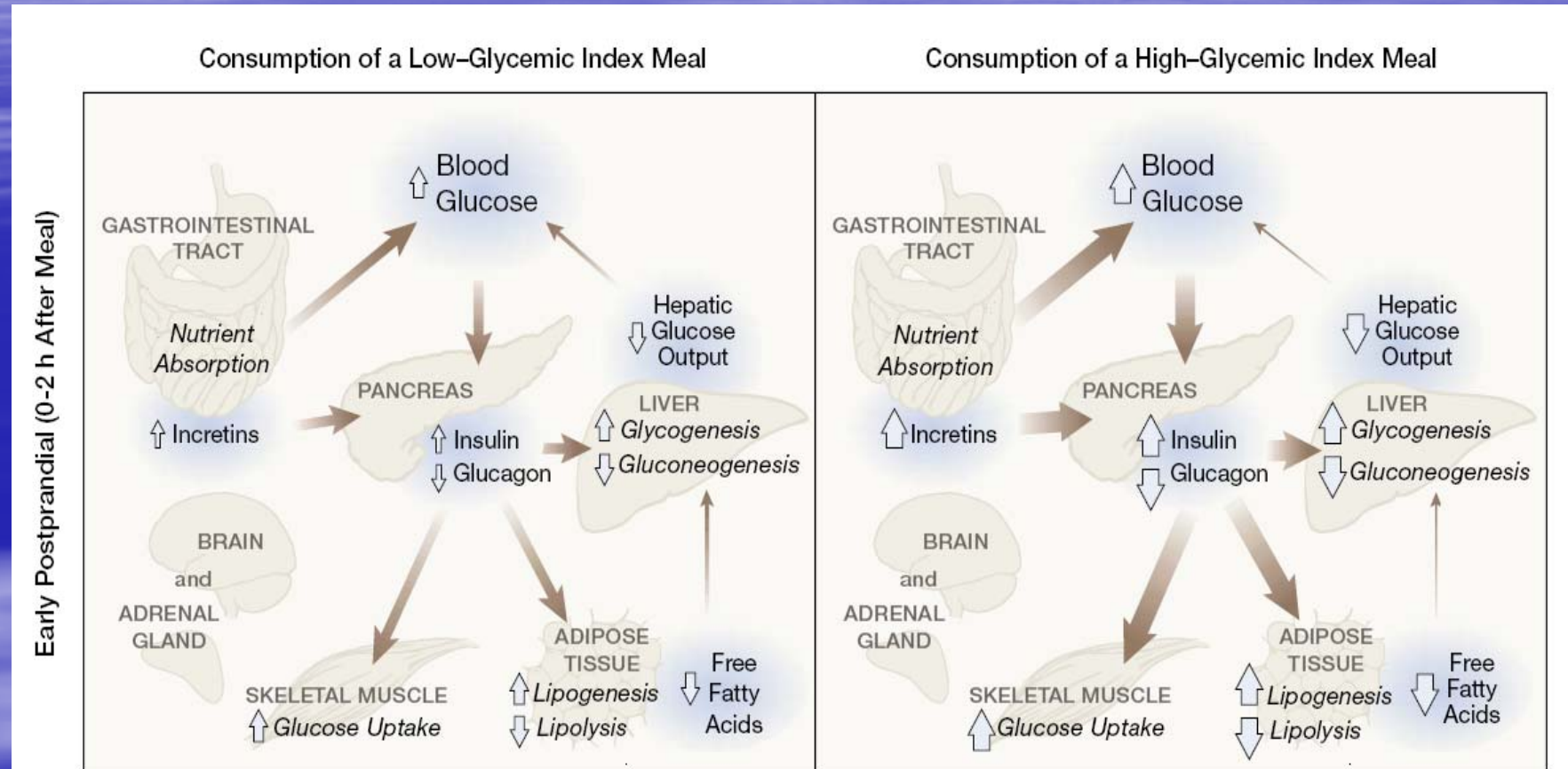
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Glycemic Index and Glycemic Load: Is the Concept Valid?



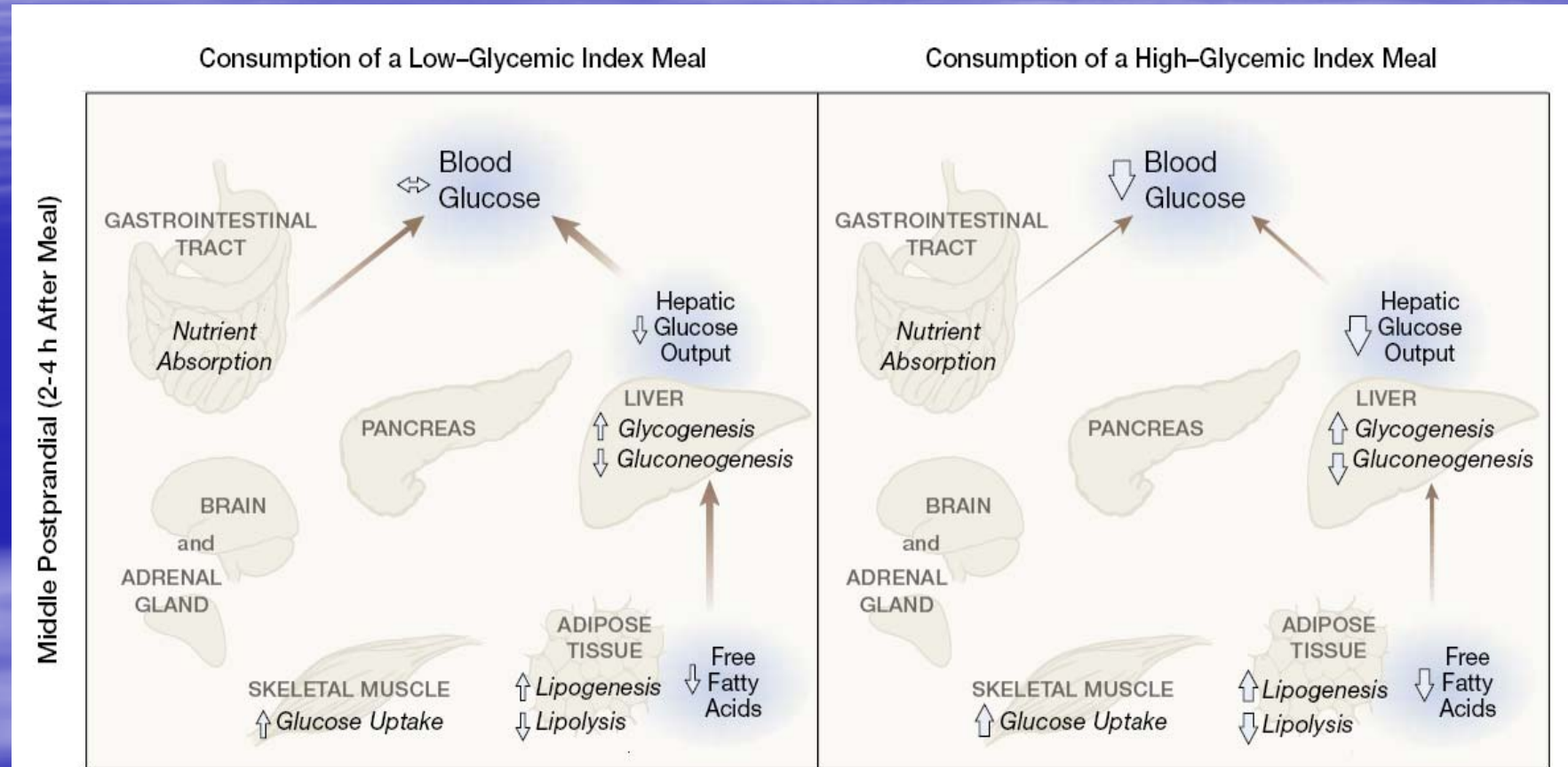
Using all the data points available, increasing glycemic load (dose level) affected the glucose response within both sets of food ($P < 0.001$). Dose and postprandial glucose response were linearly related ($P < 0.001$). Within both sets of foods, increasing glycemic load (dose level) had a significant influence on insulin response ($P < 0.001$) and a straight line adequately described the data. Profound differences were observed in postprandial insulinemia among individuals, implying greater insulin resistance in the first group.

Acute Metabolic Events following Consumption of a Meal



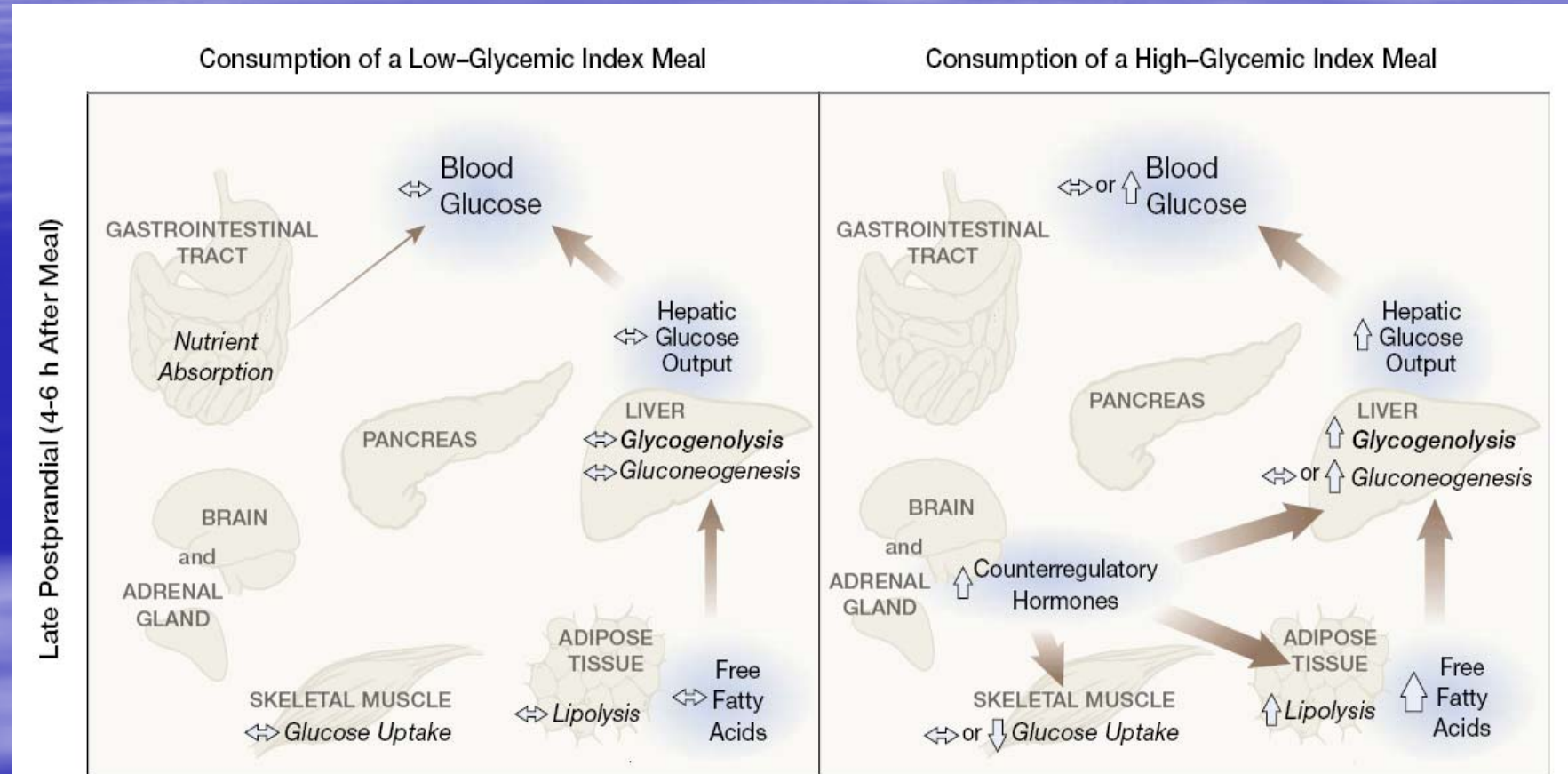
Rapid absorption of CHD after a high-GI meal results in a relatively high blood glucose level and a high insulin-to-glucagon ratio.

Acute Metabolic Events following Consumption of a Meal



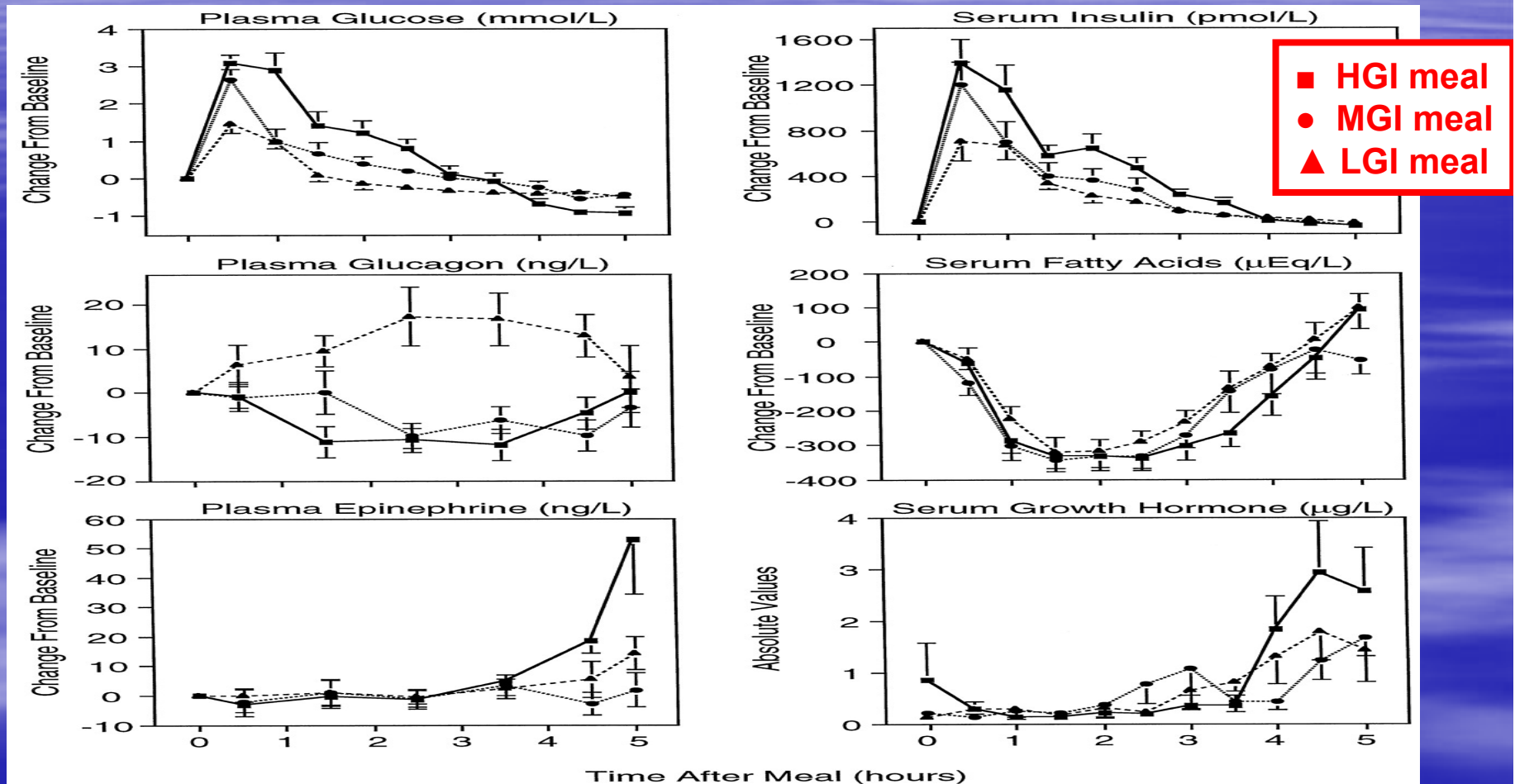
Blood glucose level decreases to below preprandial level, and free fatty acid concentration remains suppressed after a high-GI meal.

Acute Metabolic Events following Consumption of a Meal



Counterregulatory hormones after a high-GI meal restore euglycemia and cause marked increase in free fatty acid concentration.

Hormonal and Metabolic Changes after test Breakfasts



Ludwig DS et al. Pediatrics. 1999 Mar;103(3):E26

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High-GI Foods = Obesity?

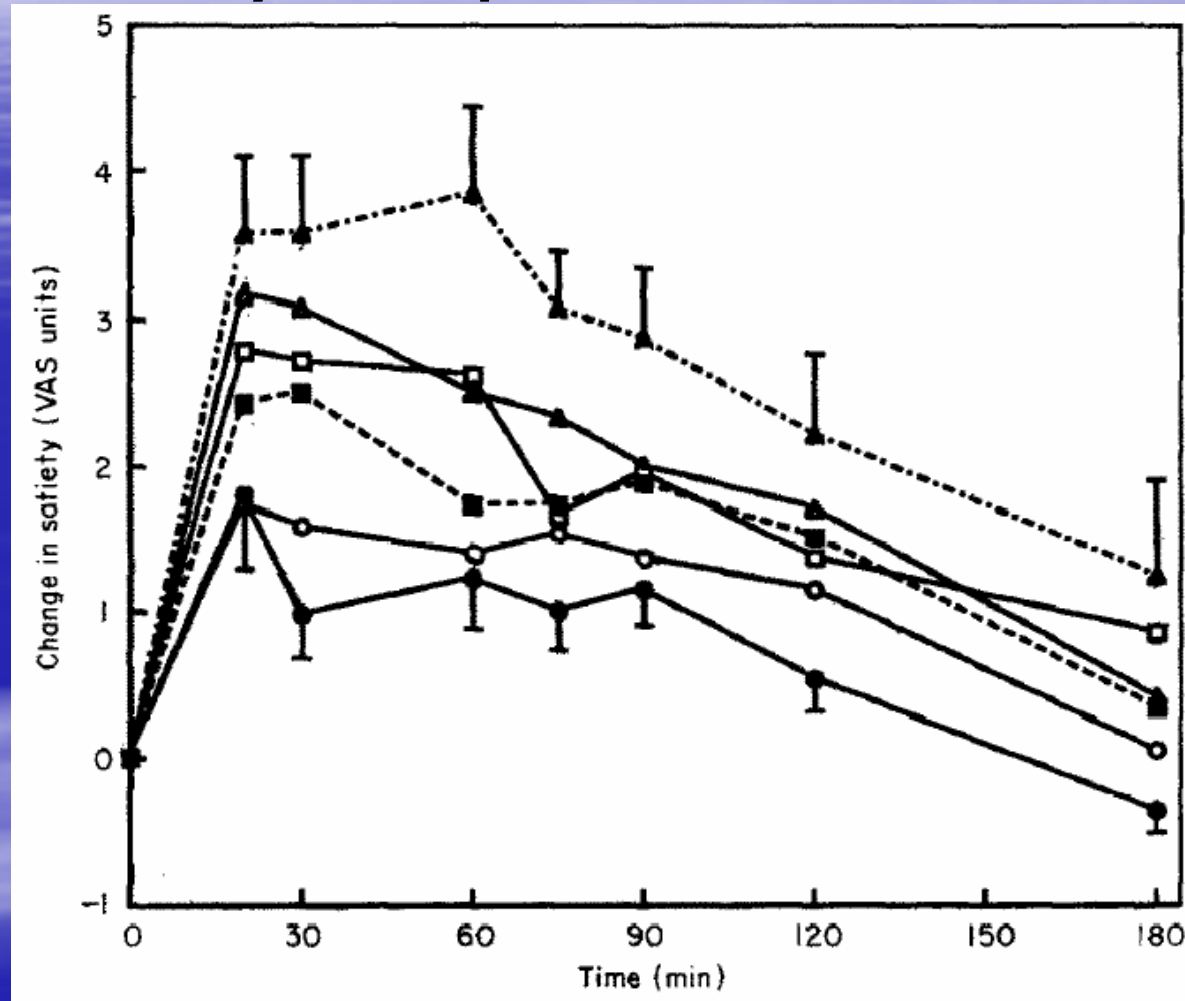
- No long-term clinical trials examining the effects of dietary GI on BW regulation
- Kabir M et al: rats fed amylopectin (HGI starch) compared with amylose (LGI starch) for 3-5 weeks exhibited larger adipocyte diameter, increased glucose incorporation into lipids, and greater fatty acid synthase
- Pawlak DB et al: animals fed a high-GI diet for 7 weeks developed increased epididymal fat mass
- Pawlak DB et al: animals fed a high-GI diet for 32 weeks developed marked obesity

Kabir M et al J Nutr. 1998 Jan;128(1):35-43

Pawlak et al J Nutr. 2001 Jan;131(1):99-104.

Pawlak DB et al Obes Res. 2000; 8:128S

Satiety Response to various Test Meals



● Rice Bubbles (116)

○ Sustain (97)

■ Vita-Brits (87)

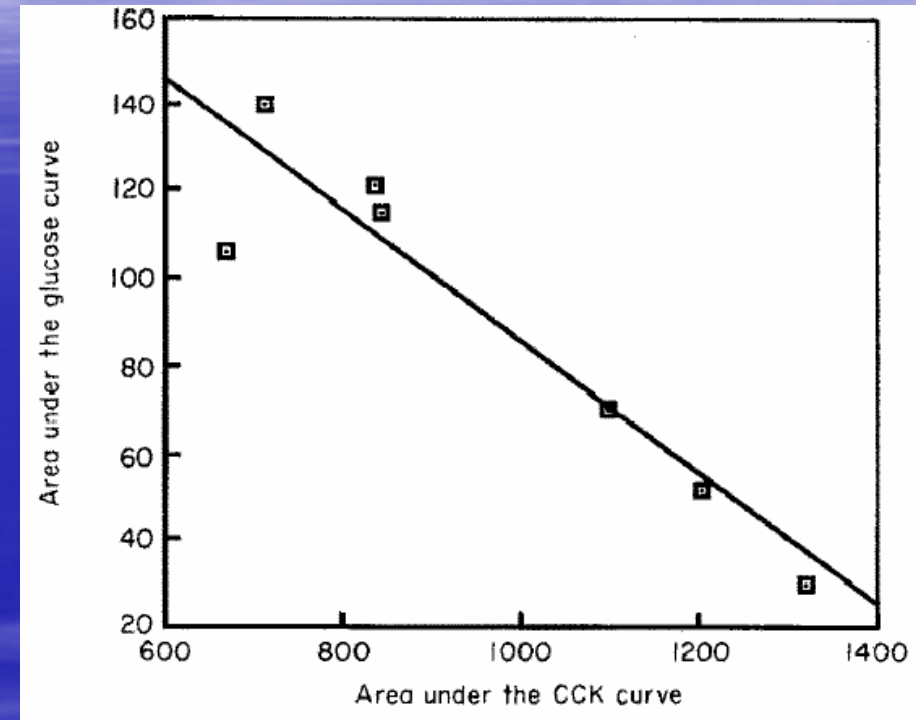
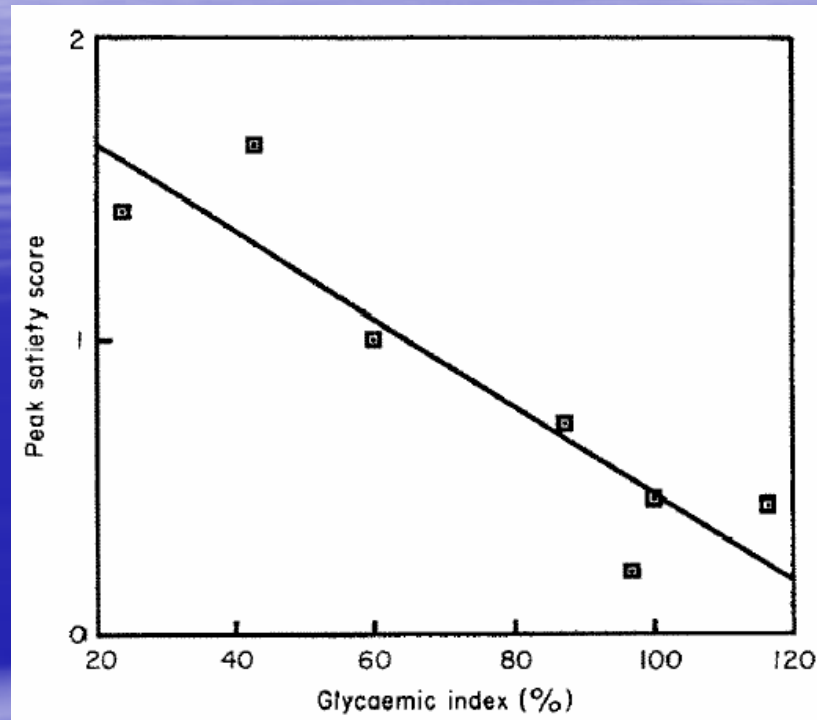
□ Porridge (59)

▲ All-Bran (42)

△ Eggs (24)

() = GI

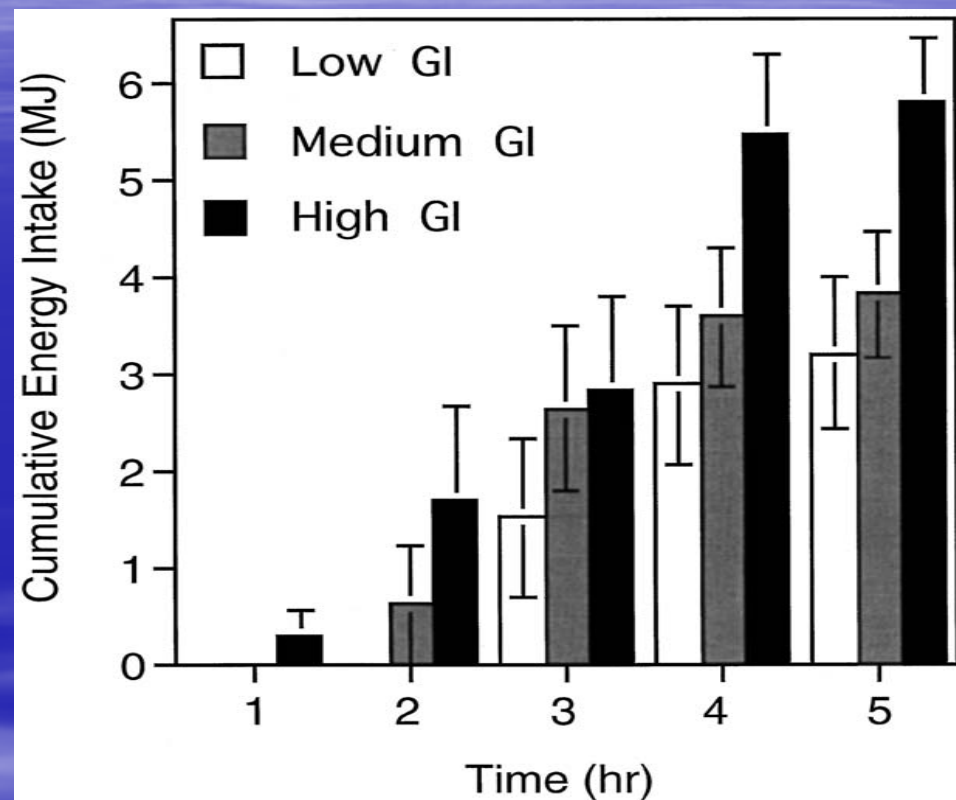
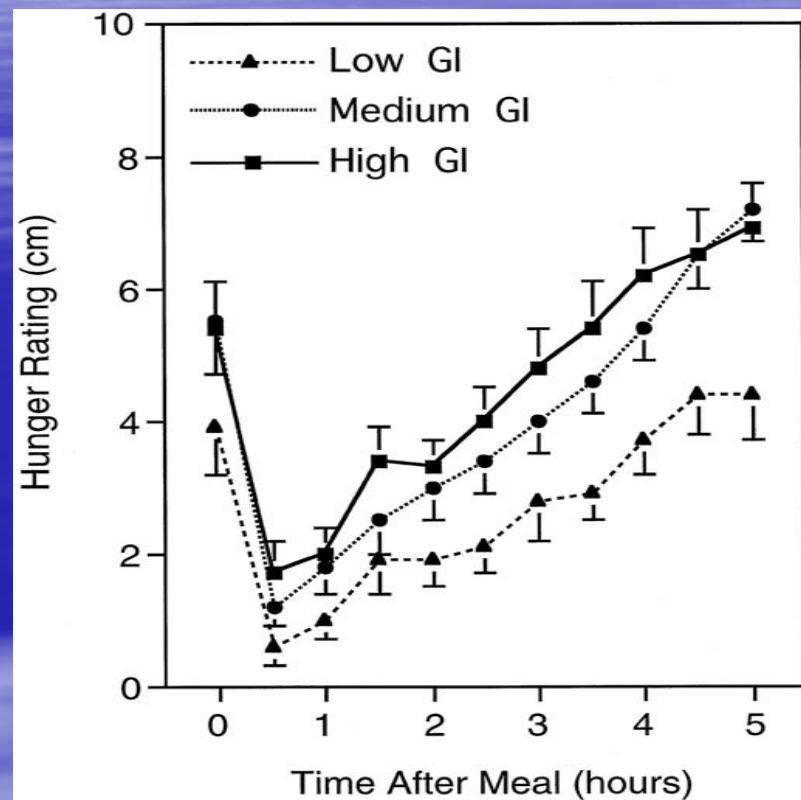
Satiety and CCK



A 50% increase in GI resulted in a 50% decrease in satiety.

Slower rates of digestion and absorption leads to prolonged anorexigenic hormonal feedback (e.g. CCK, glucagon-like-peptide 1)

Change in Hunger and cumulative Food Intake after Test Lunches



The area under the glycemic response curve was the strongest predictor of voluntary food intake. Voluntary energy intake after the HGI meal (5.8 mJ) was 53% greater than after the MGI meal (3.8 mJ), and 81% greater than after the LGI meal (3.2 mJ).

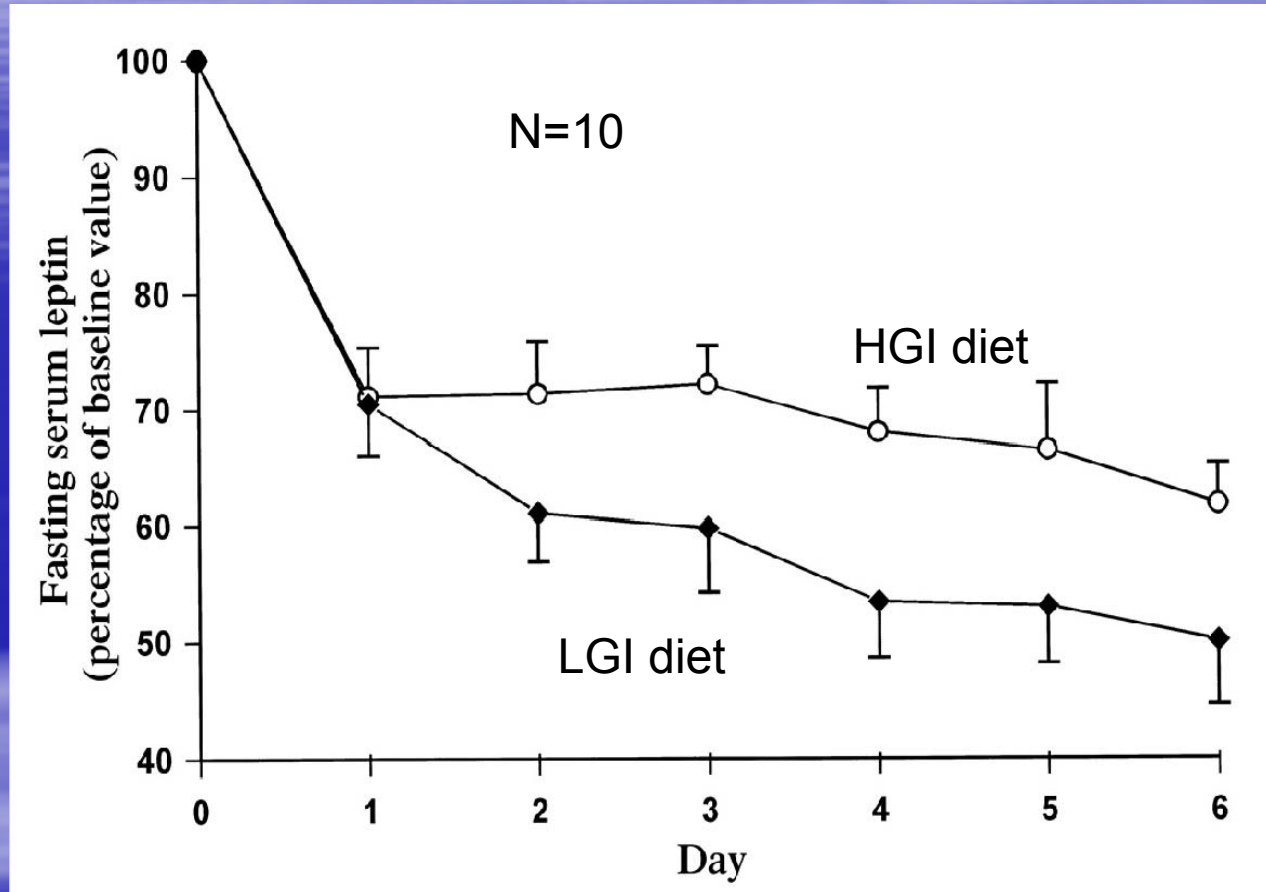
Studies comparing glycemic response with changes in hunger, satiety or energy intake

Reference	Modified dietary factor	Effect of low GI food
Haber et al. 1977 ¹	Apple, whole or processed	Increased satiety
Krotkiewski 1984	Guar gum	Decreased hunger
Spitzer and Rodin 1987	Fructose or glucose	Lower voluntary energy intake
Rodin et al. 1988	Fructose or glucose	Lower voluntary energy intake
Leathwood and Pollet 1988	Bean or potato	Decreased hunger
Rodin 1991	Fructose or glucose	Lower voluntary energy intake
Holt et al. 1992	Breakfast cereal	Increased satiety
van Amelsvoort and Westrate 1992	Amylose or amylopectin	Increased satiety
Benini et al. 1995	Fiber added to meal	Decreased hunger
Gustafsson et al. 1995a	Vegetable type	Increased satiety
Gustafsson et al. 1995b	Raw or cooked carrots	Increased satiety
Holt and Miller 1995	Rice type	Lower voluntary energy intake
Lavin and Read 1995	Guar gum	Decreased hunger
Holt et al. 1996	38 individual foods	No change in satiety
Rigaud et al. 1998	Psyllium fiber	Lower voluntary energy intake
Ludwig et al. 1999b	Oatmeal type	Lower voluntary energy intake

Ludwig DS J Nutr. 2000 Feb;130(2S Suppl):280S-283S.

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GI and Leptin



Mean (\pm SEM) daily fasting serum leptin as a percentage of baseline values.

Serum leptin decreased more rapidly and to a greater extent during the low-GI diet than during the high-GI diet ($P = 0.03$).

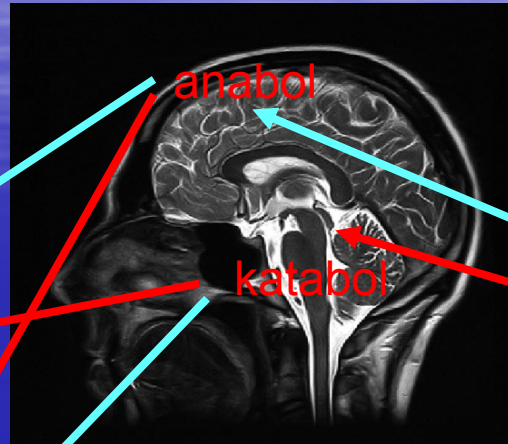
Note: Both diets had identical energy content.

Zentralnervöse Regulation der Nahrungsaufnahme - Hormone

Hohe Leptin- / Insulin-
Spiegel ↓ die
Nahrungsaufnahme
und ↑ den
Energieverbrauch



Nahrungsaufnahme



anabol

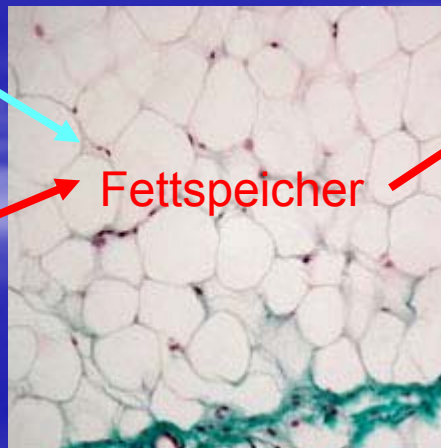
katabol

Leptin und Insulin
wirken auf
Zentralnervöse
Strukturen ein



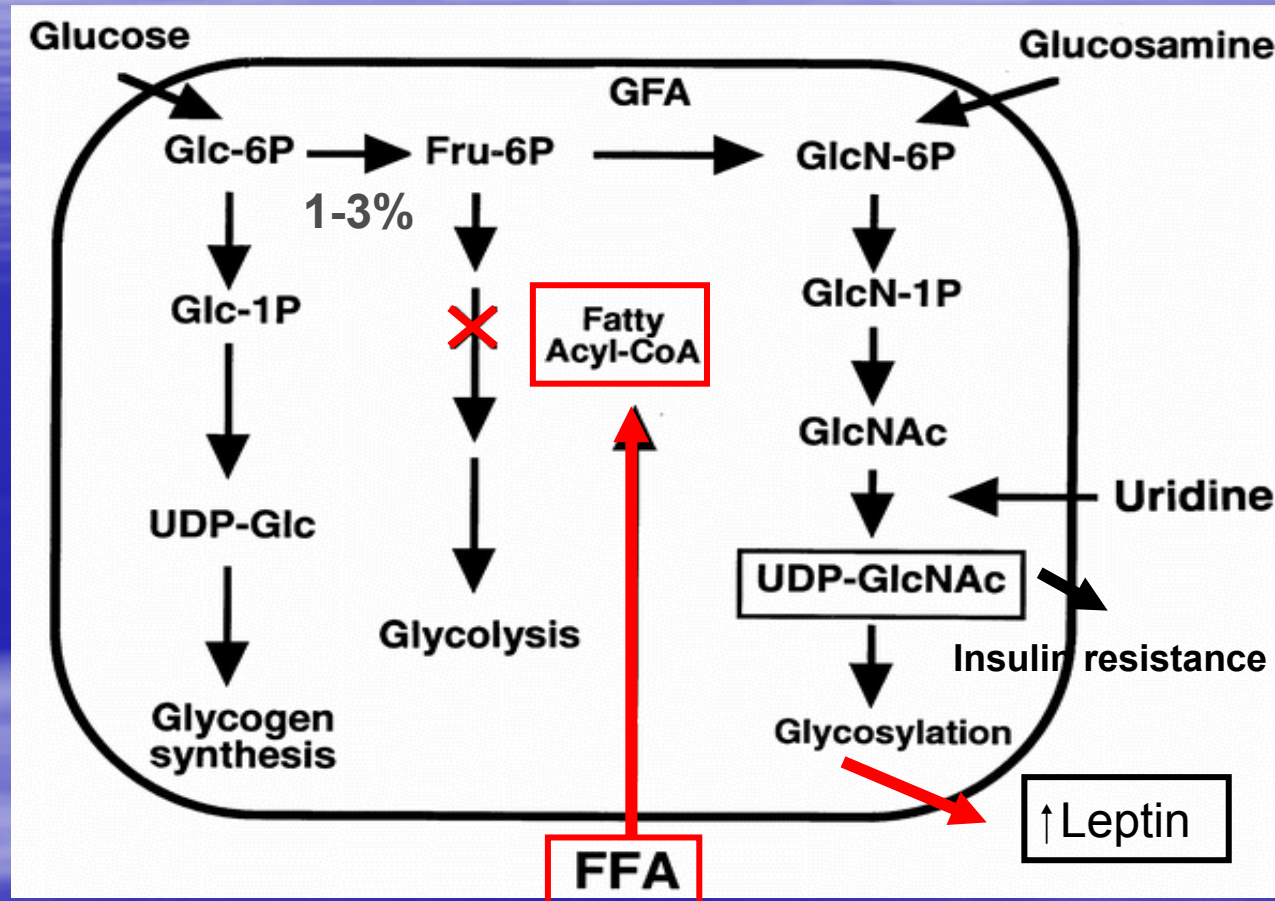
Adipositas-Signale
Leptin/Insulin

Leptin und Insulin
zirkulieren im Blut
proportional zum
Körperfettgehalt



Fettspeicher

The Hexosamine Pathway



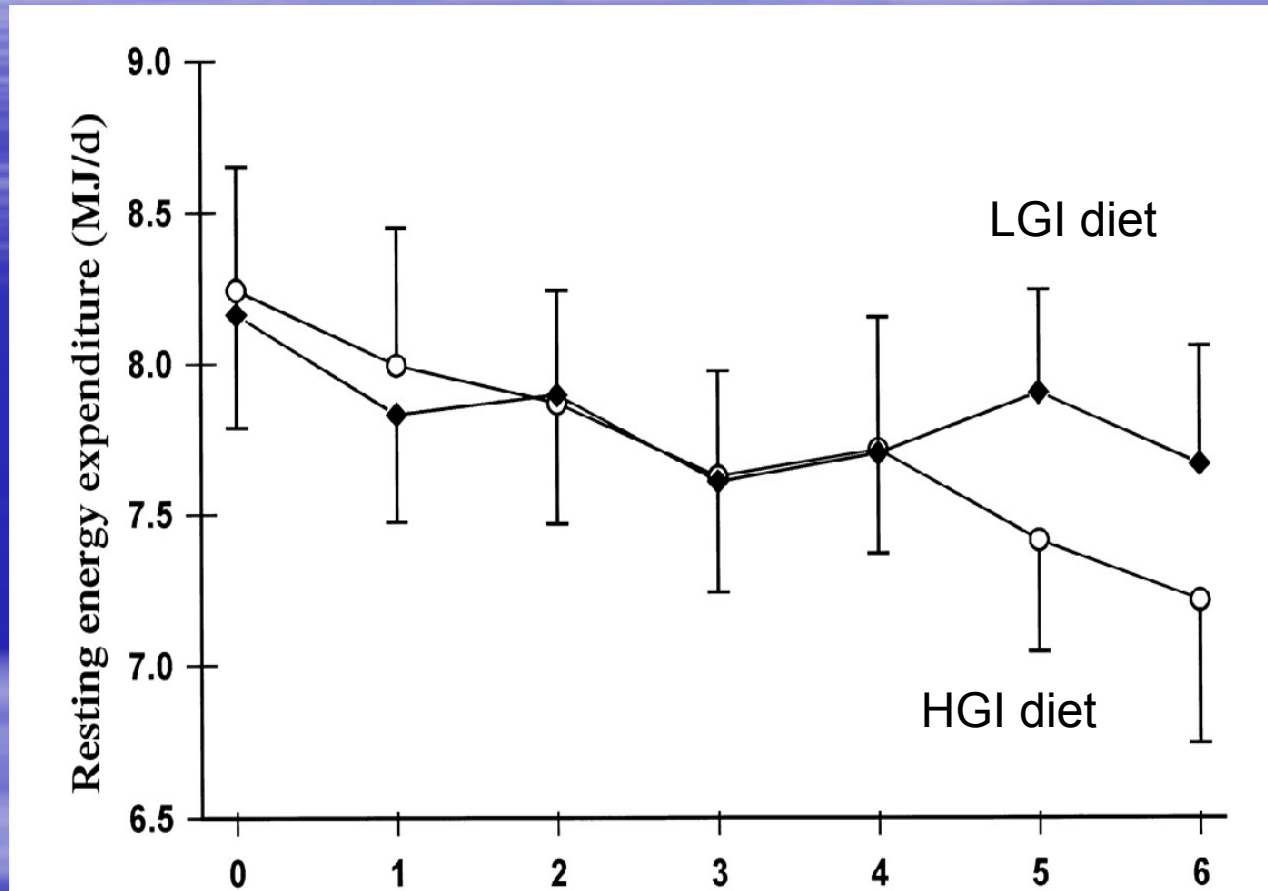
Glucose is phosphorylated to produce glucose-6-phosphate (Glc-6P), which is used mainly in glycogen synthesis and glycolysis pathways. Increased FFA availability generates increased levels of fatty-acylCoA, leading to inhibition of glycolysis. This results in increased accumulation of Fru-6P and hence increased levels of substrate for GFA.

GFA: glutamine:fructose-6-phosphate amidotransferase
 UDP-GlcNAc: UDP-N-acetylglucosamine

Wang J et al Nature. 1998 Jun 18;393(6686):684-8

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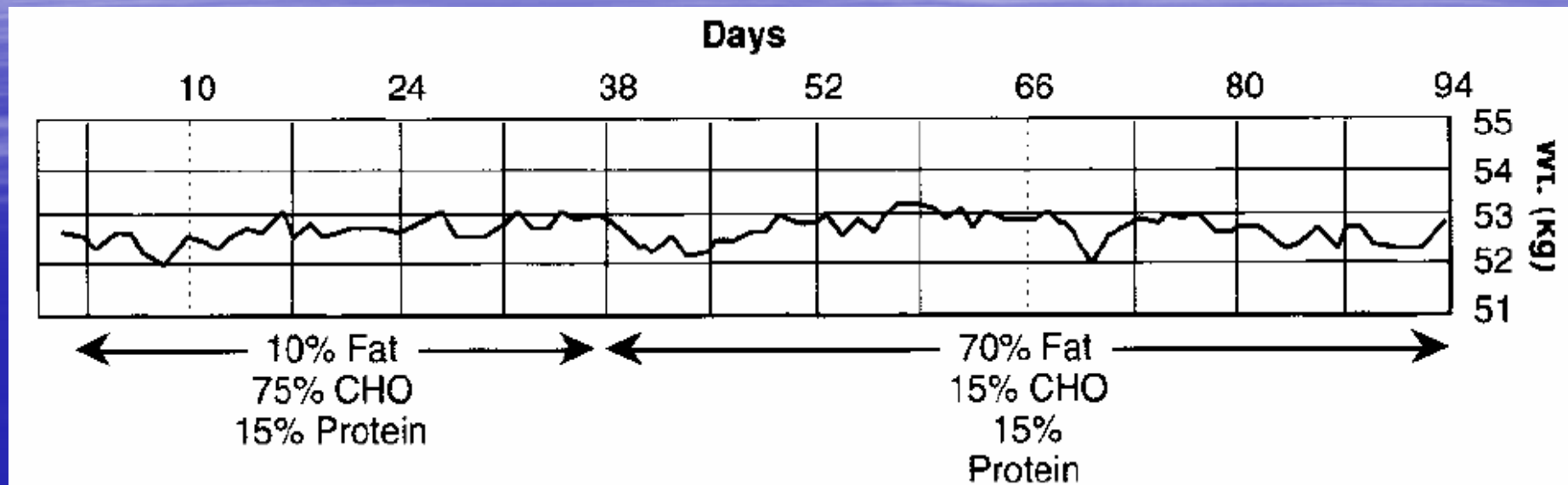
GI and REE



Mean (\pm SEM) daily resting energy expenditure with the high- (\circ) and low- (\diamond) glycemic-index diets.

REE decreased from baseline to the end of the period of energy restriction (mean of days 5 and 6) by 4.6% with the low-GI diet ($P = 0.03$) and by 10.5% with the high-GI diet ($P = 0.005$).

REE and different Meal Types



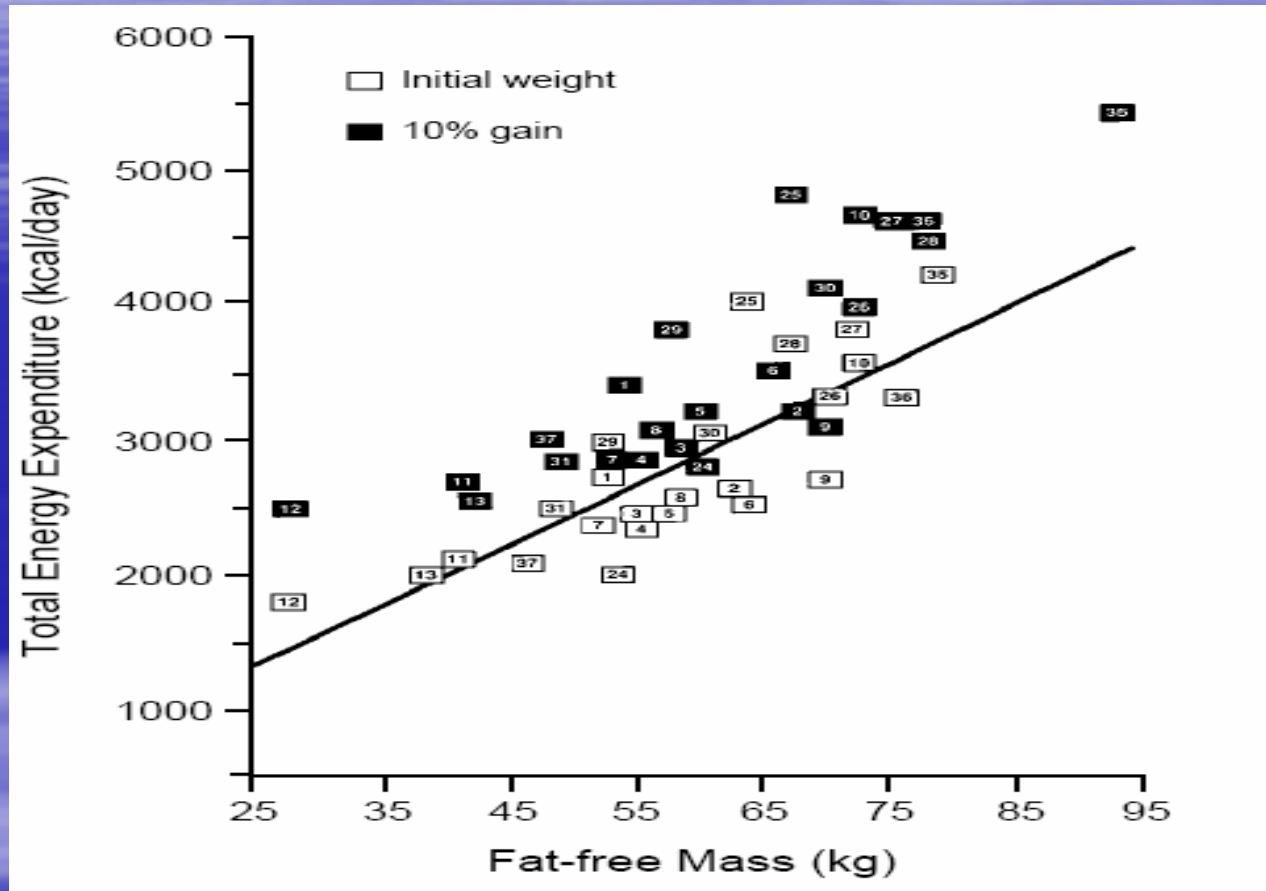
The unchanging energy need when a hospitalized patient is fed liquid diets varying widely in fat-to-carbohydrate ratio. The patient was a 64-y-old woman fed 7322 kJ/d.

Over long periods of time, different isoenergetic mixtures can fulfill the requirements for weight maintenance.

Leibel RL et al Am J Clin Nutr. 1992 Feb;55(2):350-5

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TEE and BW



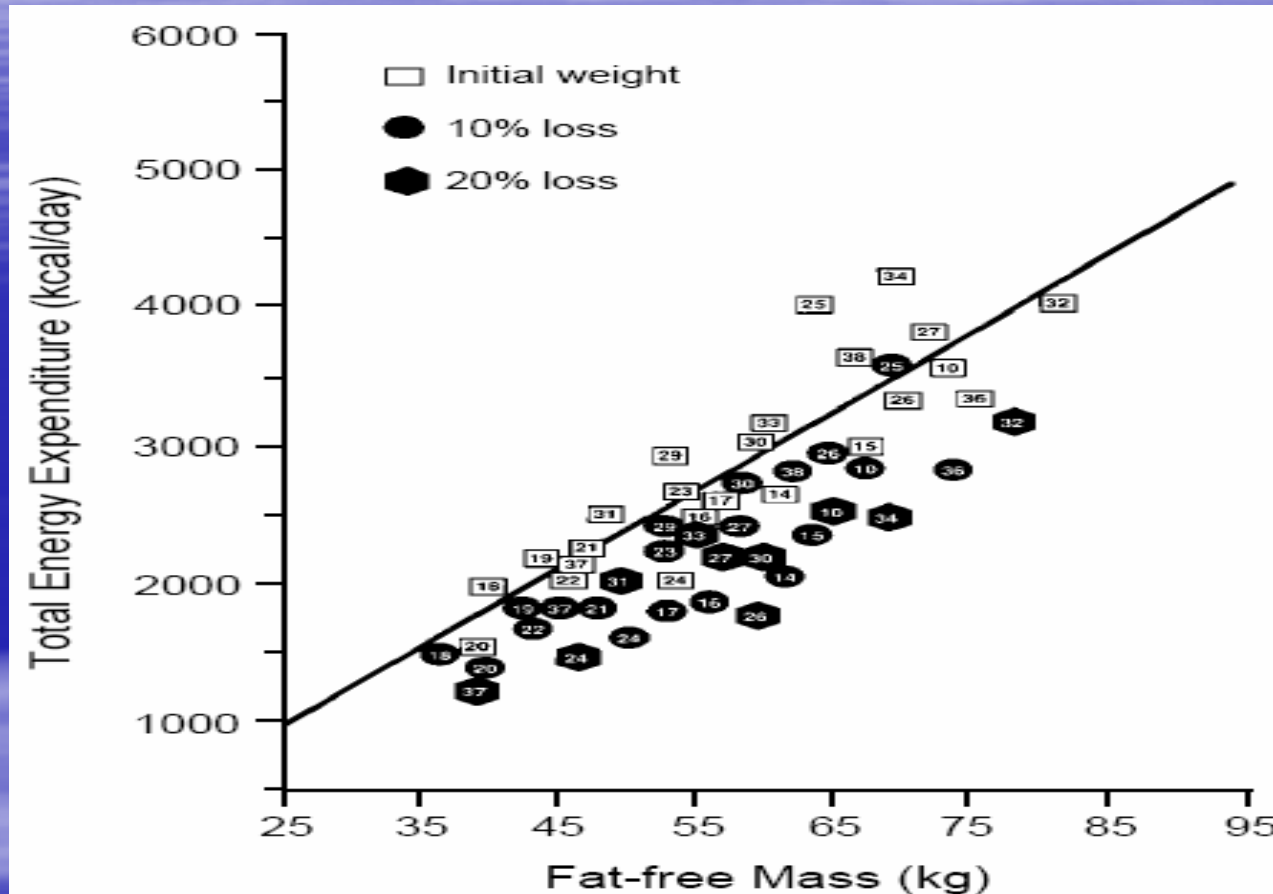
The relation of total energy expenditure (TEE), as measured by the amount of energy required to keep weight constant, with fat-free mass (FFM).

A 10 percent increase in the usual weight was accompanied by a 16 percent increase in 24-hour total energy expenditure.

Leibel RL et al N Engl J Med. 1995 Mar 9;332(10):621-8

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TEE and BW



The relation of total energy expenditure (TEE), as measured by the amount of energy required to keep weight constant, with fat-free mass (FFM).

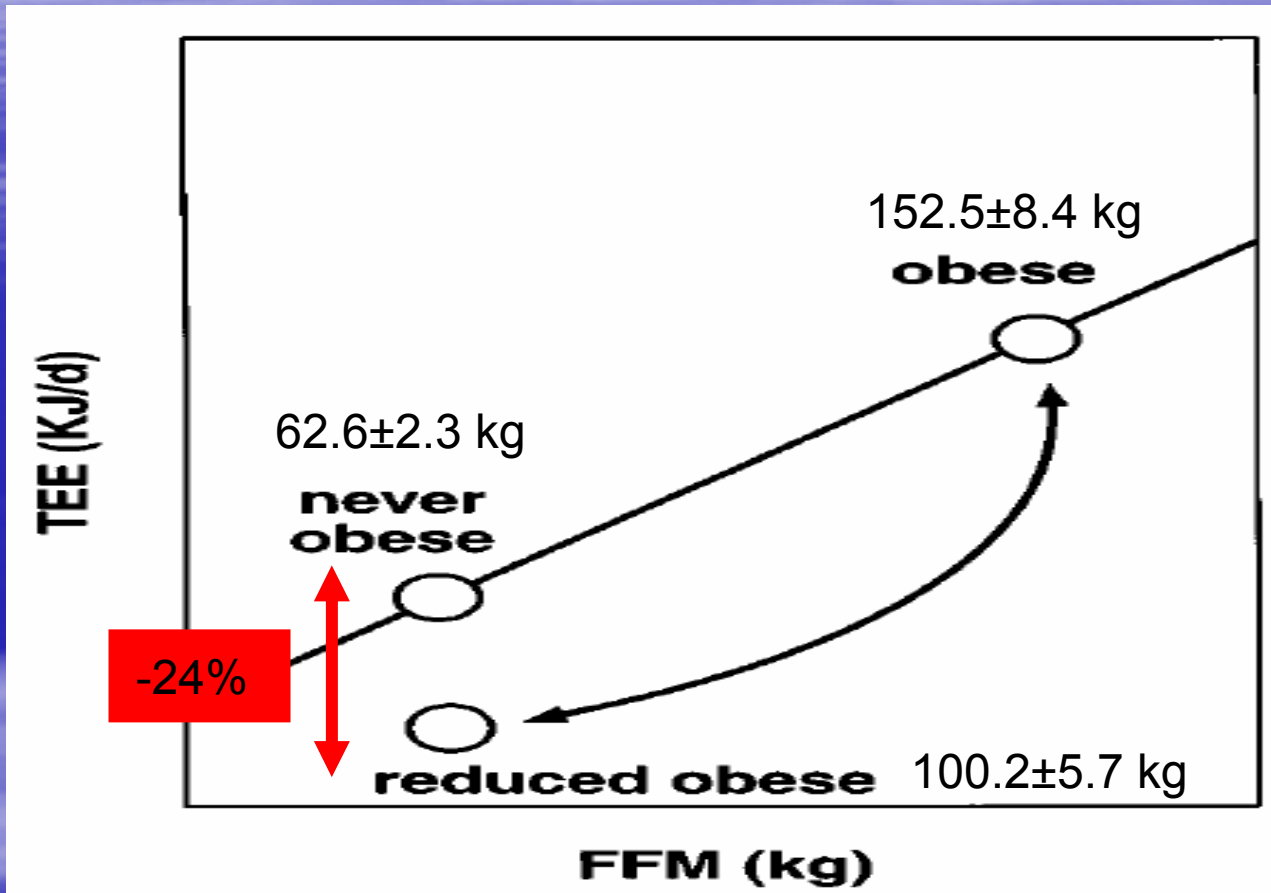
There were no significant differences in energy expenditure at weights 10 and 20 percent below the initial weight, suggesting that the maximal adaptation to the maintenance of a reduced body weight was already attained at the 10 percent level.

A 10 percent decrease in the usual weight was accompanied by a 15 percent decrease in 24-hour total energy expenditure.

Leibel RL et al N Engl J Med. 1995 Mar 9;332(10):621-8

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TEE and BW



The mean individual energy requirement of the reduced-obese subjects (2171 kcal/d) was less than that for the control subjects (2280 kcal/d) despite the fact that they still weighed 60% more than the controls.

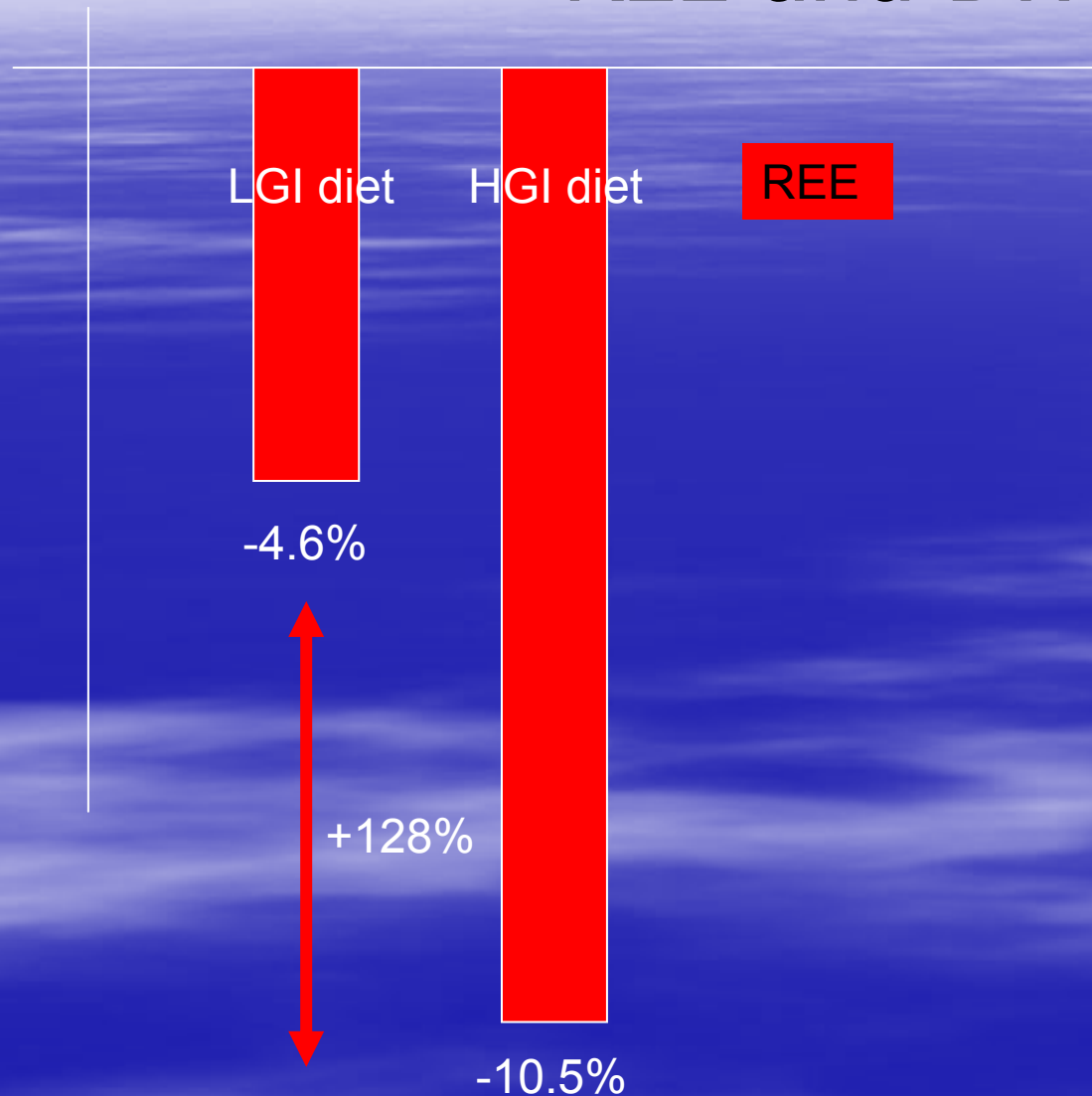
Leibel RL, Hirsch J Metabolism. 1984 Feb;33(2):164-70

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A hypothetical schema suggesting one reason for the high recidivism rate after weight reduction.

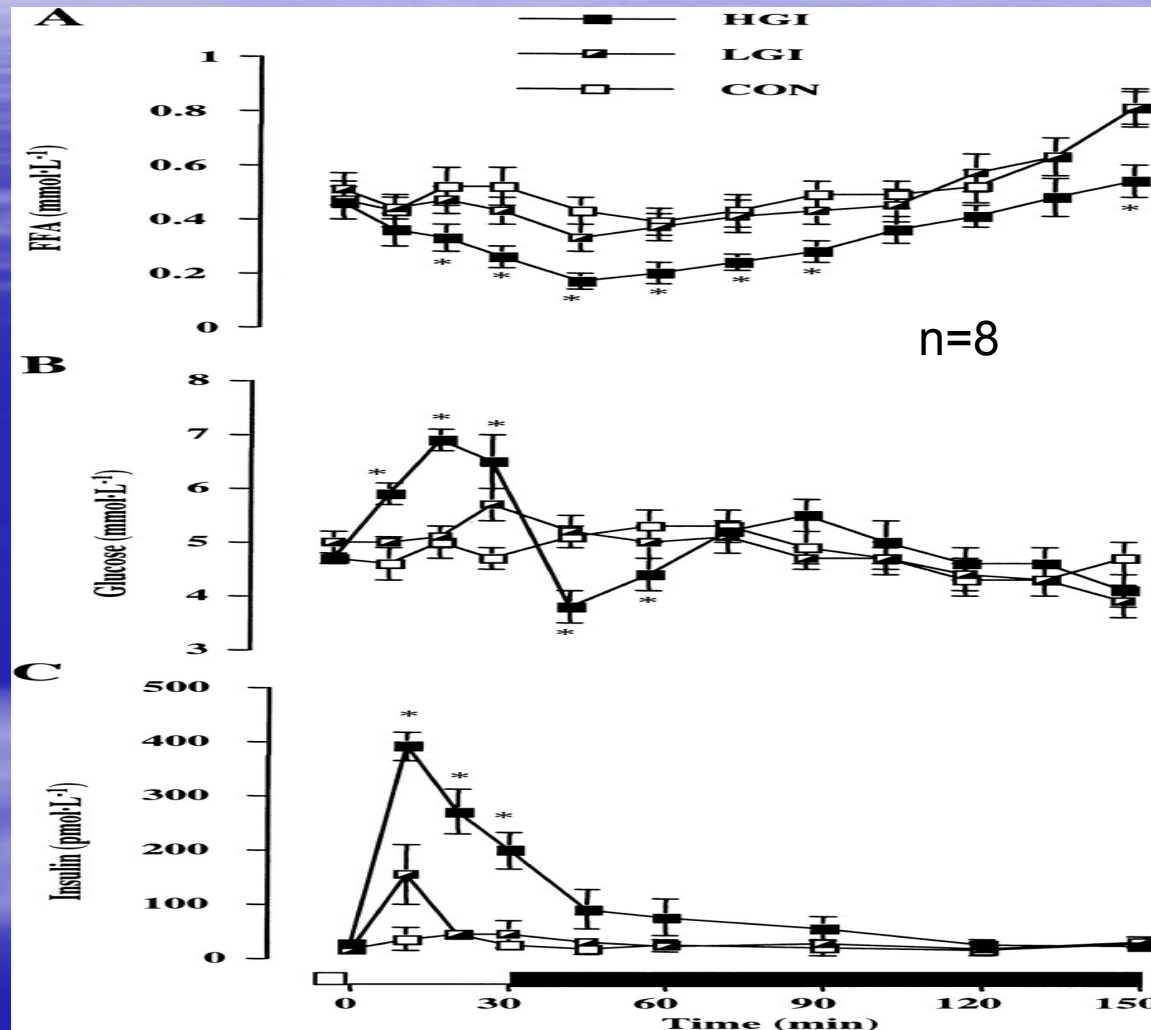
Following weight loss, the reduced-obese subjects required only 1021 +/- 32 kcal/m²/d, a 28% decrease (P<0.001) in requirements relative to their obese state and a 24% decrease relative to the control patients (P<0.001).

REE and BW



Agus MS and colleagues found a reduction of REE from baseline to the end of the period of energy restriction (mean of days 5 and 6) by 4.6% with the LGI diet ($P = 0.03$) and by 10.5% with the HGI diet ($P = 0.005$), which amounts to a plus of 128% with the HGI diet.

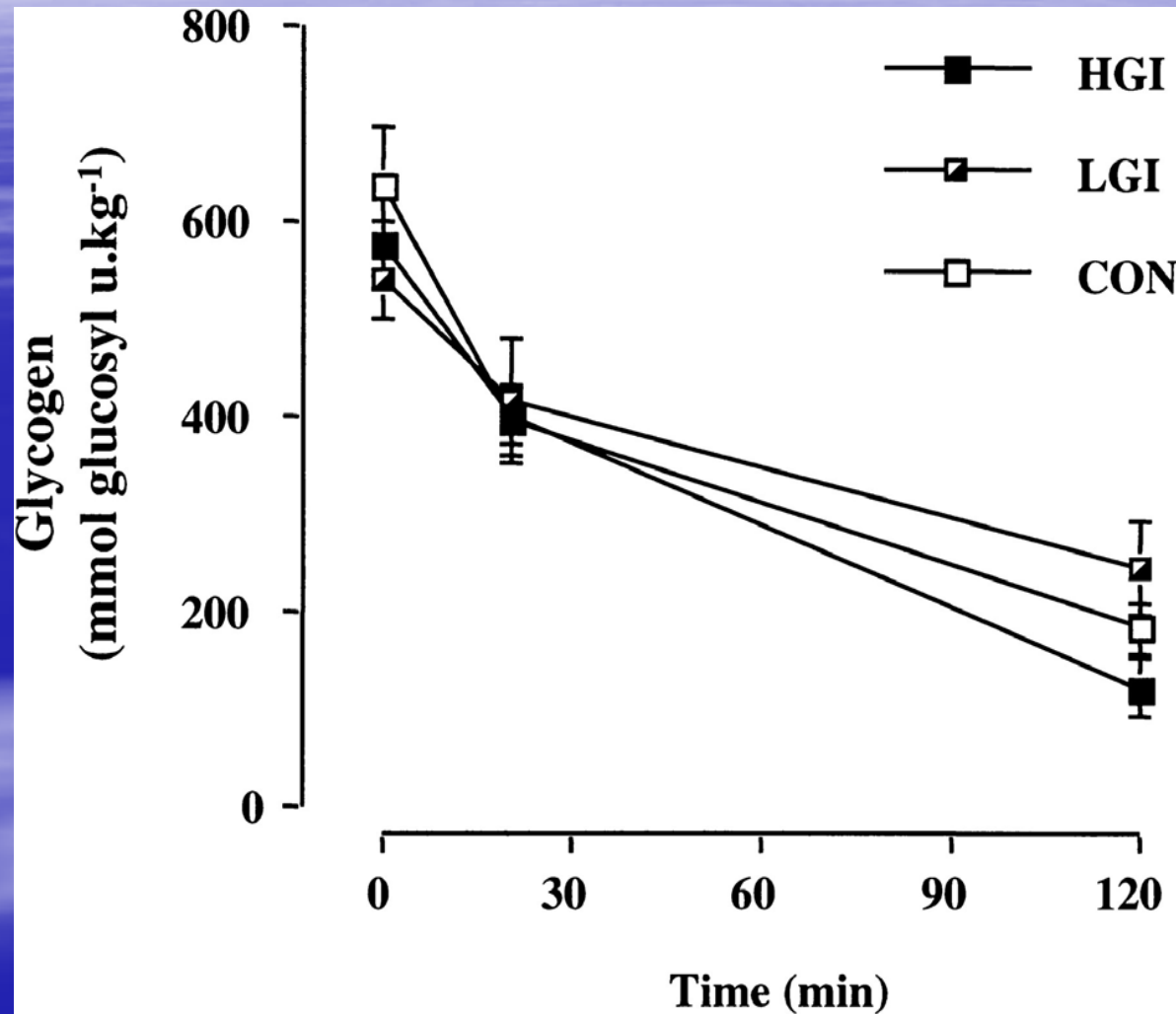
Glucose Index and Fat Utilization



Plasma free fatty acid (FFA; A), glucose (B), and insulin (C) concentrations at rest and during submaximal exercise with the ingestion of a high-glycemic index (HGI), low-glycemic index (LGI), and placebo (Con) meal

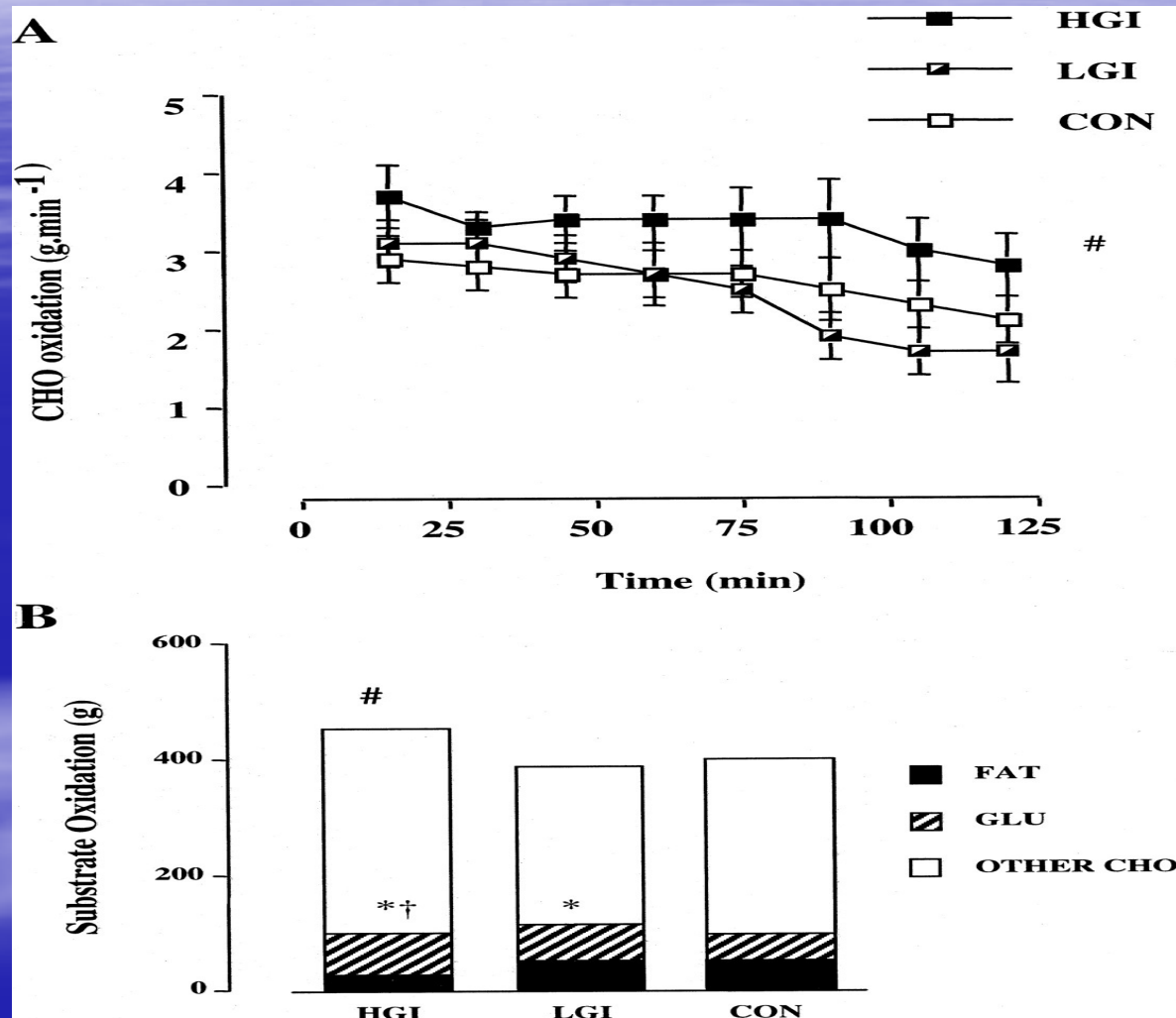
LGI meal: muesli
HGI meal: mashed potatoes
Con meal: diet jelly

Glucose Index and Fat Utilization



Muscle glycogen before (0 min), during (20 min), and after (120 min) submaximal exercise with the ingestion of a HGI, LGI, and Con meal

Glucose Index and Fat Utilization



Rate of carbohydrate (CHO) oxidation (A) and total substrate oxidation (B) with the ingestion of a HGI, LGI, and Con meal

Ways through which LGI Foods may promote Weight Control

- Promoting satiety
 - Longer transit time results in prolonged feedback time of anorexigenic hormones to the satiety center in the brain
- Promoting fat oxidation at the expense of CHO oxidation
 - Acute increase in glucose and insulin leads to activation of CHO oxidation through the rapid activation of key-rate limiting enzymes
 - e.g. malonyl-CoA, an intermediate of glucose oxidation, strongly inhibits fatty acid transport into mitochondria, resulting in decreased fatty acid oxidation
 - Chronic hyperglycemia and hyperinsulinemia alters the expression of key-rate limiting enzymes (e.g. carnitine palmitoyl transferase) and, thus, fat oxidation
 - Simoneau JA et al: in obesity-related insulin resistance, the metabolic capacity of skeletal muscle appears to be organized toward fat esterification rather than oxidation and dietary-induced weight loss does not correct this disposition

Brand-Miller JC et al Am J Clin Nutr. 2002 Jul;76(1):281S-5S

Simoneau JA et al FASEB J. 1999 Nov;13(14):2051-60

Weyer C et al J Clin Endocrinol Metab. 2000 Mar;85(3):1087-94

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Short-term Responses to high- and low GI Foods

- Lower decrease of serum leptin with HGI diet
 - Insulin acts as a leptin secretagogue
 - HGI foods lead to an increased intracellular glucose metabolism and an increased lipogenesis
 - Activation of hexosamine biosynthetic pathway leads to increased insulin resistance and serum leptin
- Probable functional improvement of leptin resistance associated with obesity might explain why albeit lower energy intakes with LGI foods satiety levels are higher
- REE decreases to a lesser extent with the LGI than with the HGI diet
 - Protein content of the diet?
 - Sleeping metabolic rate decreases more rapidly with a low-protein compared with a high-protein diet
 - Set point theory?
- Nitrogen balance is positive with a LGI diet and negative with a HGI diet
 - Counterregulatory hormones (e.g. cortisol) may have proteolytic actions

Agus MS et al Am J Clin Nutr 2000;71:901-7

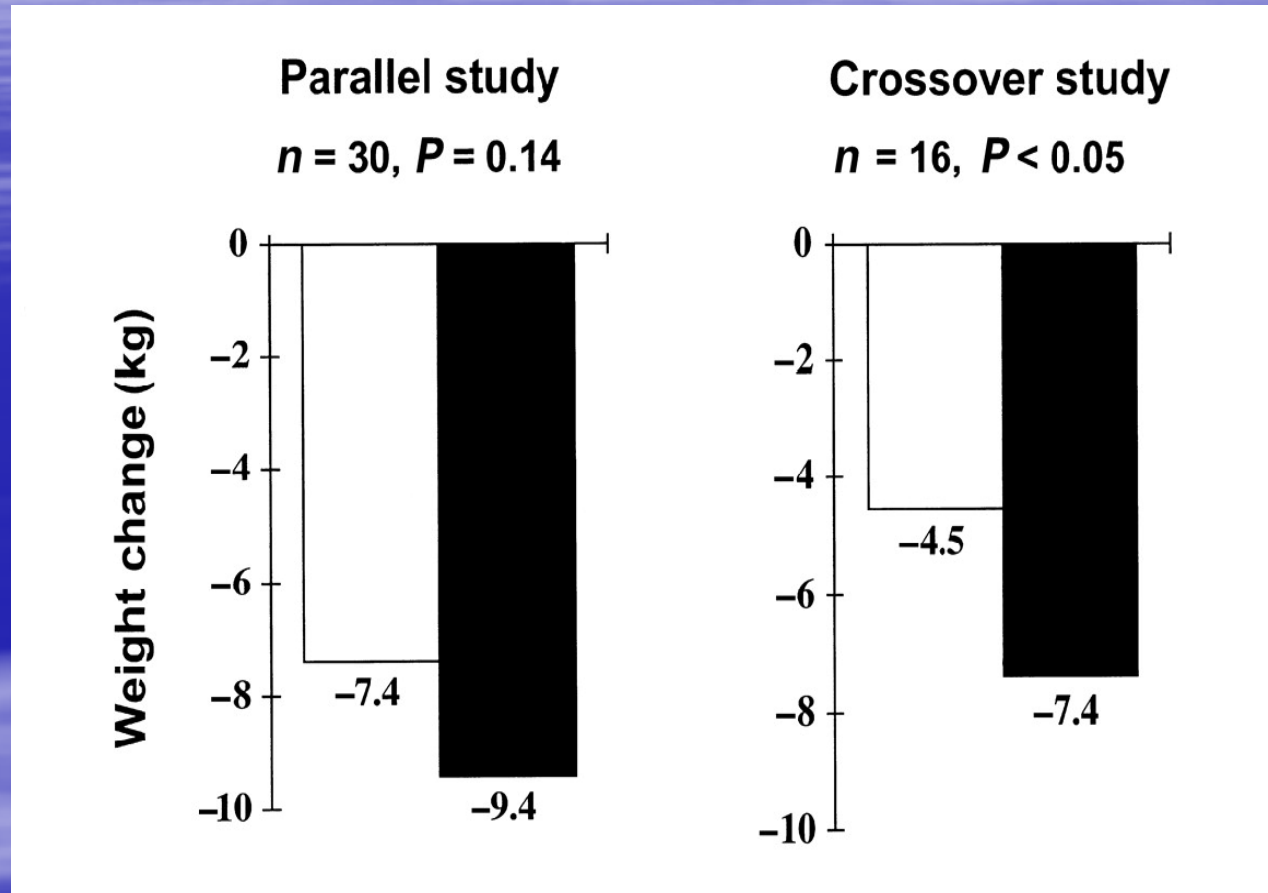
Wang J et al Nature. 1998 Jun 18;393(6686):684-8

Gelfand RA et al J Clin Invest. 1984 Dec;74(6):2238-48

Howe et al J Nutr. 1996 Sep;126(9):2120-9

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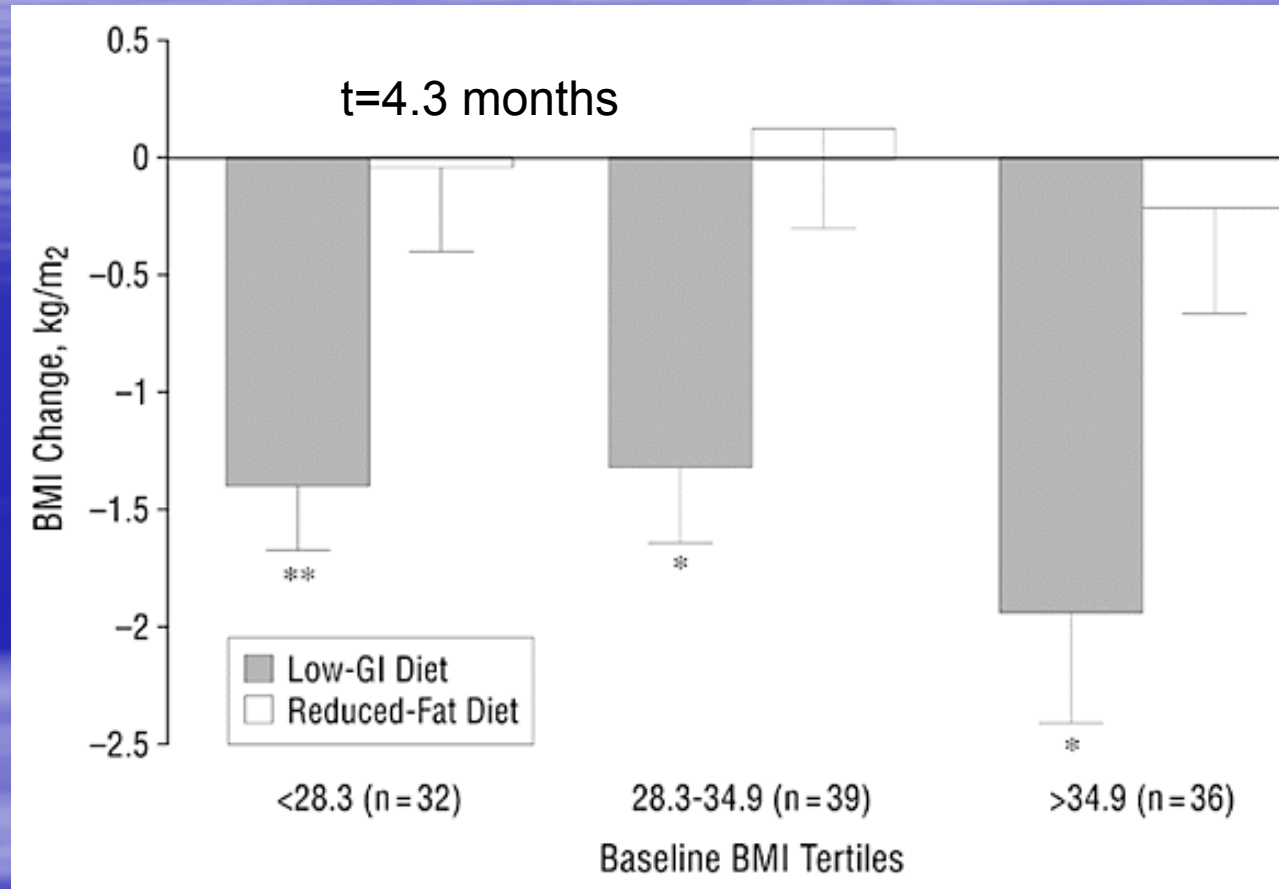
GI and Weight loss: Medium-term effects



Weight loss during a parallel and crossover study of overweight women randomly assigned to consume high-GI (□) or low-GI (■) diets for 12 wk each .

In both arms, the reduction in fasting insulin concentrations was greater with the low-GI diet than with the isoenergetic, macronutrient-balanced, high-GI diet.

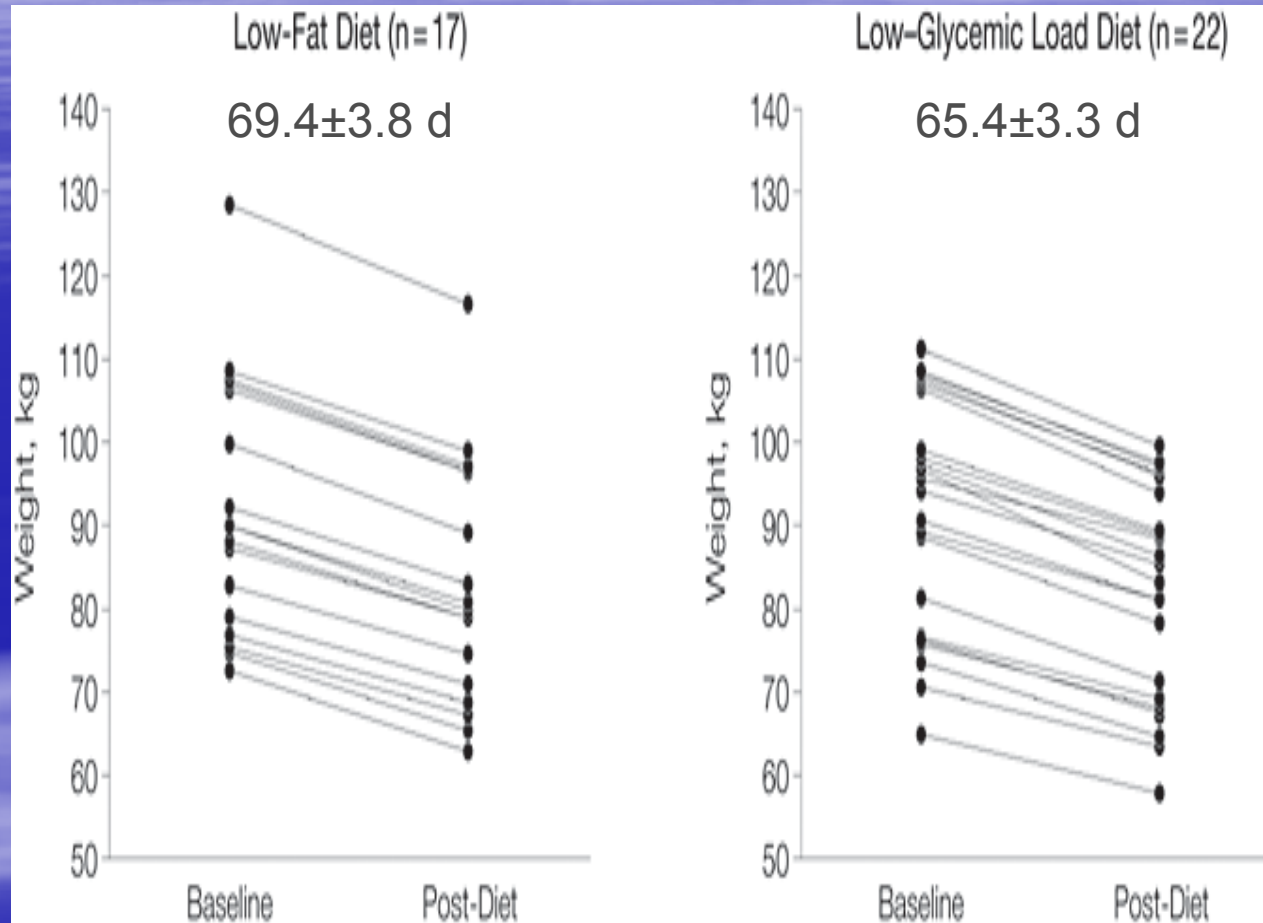
GI and Weight loss: Medium-term effects



Mean \pm SE changes in body mass index (BMI) by dietary treatment according to tertiles of baseline BMI. One asterisk indicates $P<.05$; 2 asterisks, $P<.01$.

BMI and body weight decreased more in the low-GI group than in the conventional diet group, even after adjustment for age, sex, ethnicity, baseline BMI, and baseline weight.

GI and Weight loss: Medium-term effects

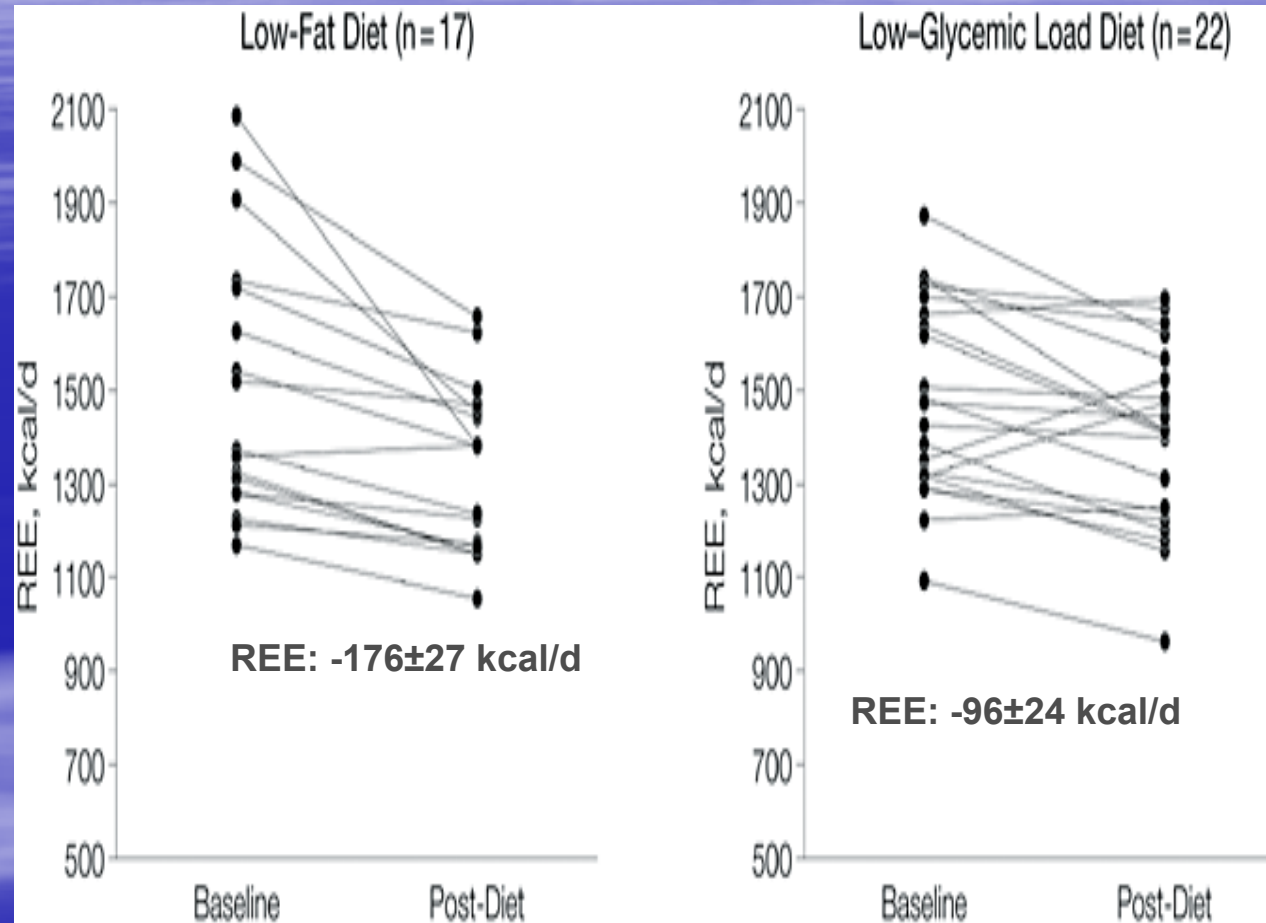


Individual rates of weight loss were nonsignificantly greater in the low-glycemic load compared with the low-fat groups (1.09 [0.05] vs 0.99 [0.05] kg/wk, $P = .19$).

Body weight for each participant at baseline and post-diet for the low-fat and low-glycemic load diet groups .

Per study design, all participants who completed the protocol lost approximately 10% of their initial body weight. The mean (SE) time between the baseline and post-weight loss clinic visits was 69.4 (3.8) days for lowfat and 65.2 (3.3) days for low-glycemic load groups ($P=.41$ for treatment effect).

GI and Weight loss: Medium-term effects



Resting energy expenditure (REE) for each participant at baseline and post-diet for the low-fat and low-glycemic load diet groups.

The group specific difference in energy balance amounted to 80 kcal/d, which corresponds to approx. 1.5 km of walking/d.

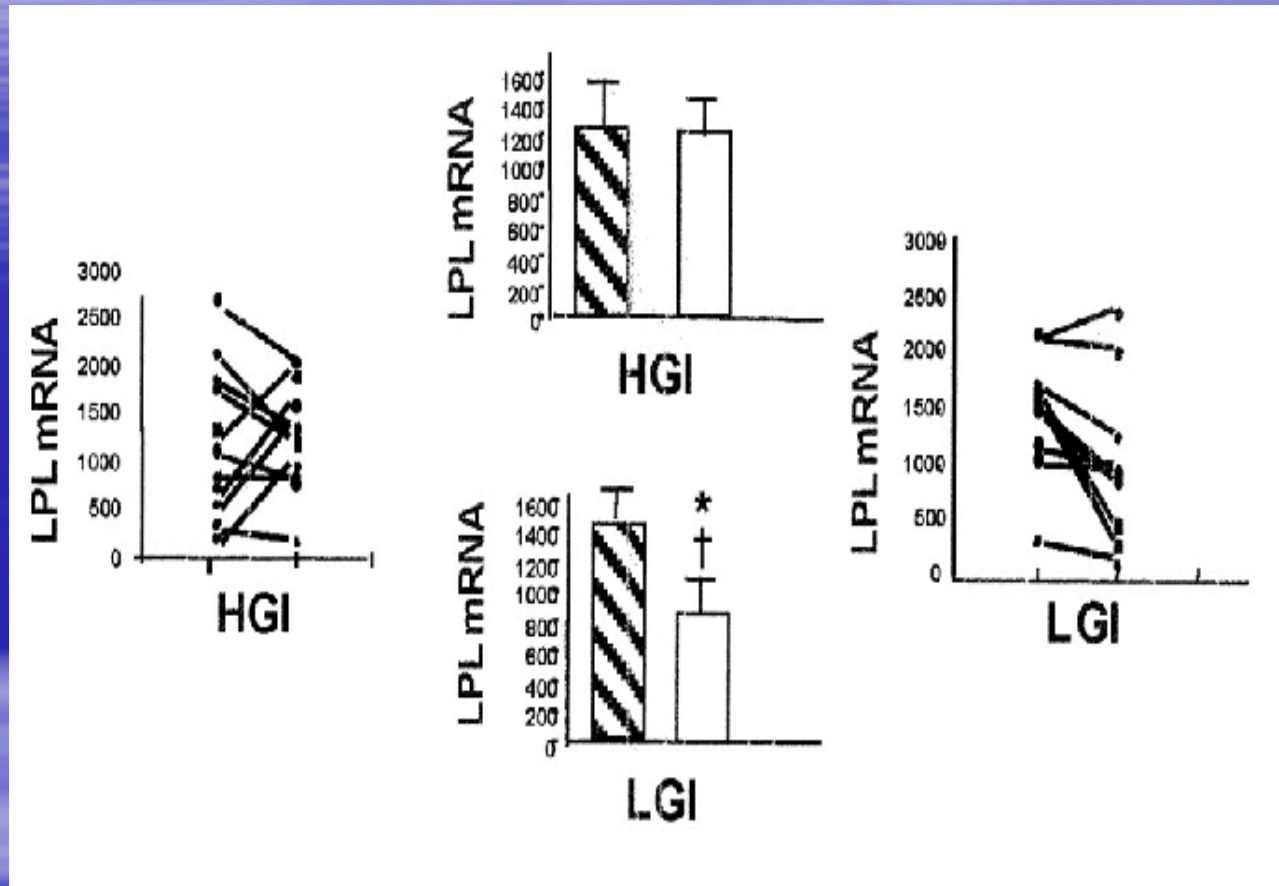
Resting energy expenditure decreased less in the low-glycemic load group compared with low-fat group following weight loss (5.9% [1.5%] vs 10.6% [1.7%], $P = .05$).

GI and Weight loss: Medium-term effects

	HGI diet		LGI diet	
	Baseline	5 Weeks	Baseline	5 Weeks
Total cholesterol				
Fasting (0 min; mmol/l)	5.52 ± 0.42	5.30 ± 0.39	5.30 ± 0.27	4.90 ± 0.38#
Morning AUC (mmol/min)	886 ± 61	824 ± 55	845 ± 47	762 ± 55†
Afternoon AUC (mmol/min)	897 ± 68	782 ± 0	874 ± 61	768 ± 57
Triacylglycerols				
Fasting (0 min; mmol/l)	1.33 ± 0.15	1.37 ± 0.22	1.59 ± 0.25	1.50 ± 0.42
Morning AUC (mmol · l ⁻¹ · 4 h ⁻¹)	292 ± 40	272 ± 47	336 ± 38	336 ± 62
Afternoon AUC (mmol · l ⁻¹ · 4 h ⁻¹)	334 ± 43	376 ± 55	413 ± 49	335 ± 36‡*
FFA (0 min; mmol/l)	0.31 ± 0.02	0.32 ± 0.04	0.32 ± 0.03	0.39 ± 0.06
HDL cholesterol (mmol/l)	1.06 ± 0.09	1.06 ± 0.01	0.98 ± 0.08	1.01 ± 0.08
LDL cholesterol (mmol/l)§	4.01 ± 0.26	3.74 ± 0.21	3.71 ± 0.16	3.35 ± 0.32
ApoA (g/l)	1.5 ± 0.09	1.45 ± 0.08	1.45 ± 0.08	1.44 ± 0.09
ApoB (g/l)	1.28 ± 0.08	1.2 ± 0.07	1.21 ± 0.07	1.14 ± 0.06†
Total fat mass (kg)	19.54 ± 1.52	19.52 ± 1.57	19.27 ± 1.69	18.75 ± 1.59 ‡*
Trunk fat (kg)	9.32 ± 0.86	8.92 ± 0.88	8.70 ± 0.93	8.41 ± 0.86 **

Five weeks of the LGI diet, compared with the same period of the HGI diet, induced a reduction of 700 g of total fat mass for eight subjects and >1 kg for five subjects. During the LGI diet, there was a gain of 430 ± 143 g of lean mass.

GI and Weight loss: Medium-term effects



Levels of LPL mRNAs in abdominal subcutaneous adipose tissue before (baseline: left column) and after 5 weeks (right column) of HGI and LGI diets. * $P < 0.05$.

LPL was decreased at the end of the 5-week LGI diet by 33% ($1,415 \pm 153$ vs. 959 ± 202 amol/ μ g total RNA; $P < 0.05$).

PPAR- γ mRNA quantity was not modified by the type of diet (HGI: 20.7 ± 3.4 vs. 18.0 ± 2.7 ; LGI: 21.8 ± 4.1 vs. 22.1 ± 4.0 , baseline vs. 5 weeks).

GI and Weight loss: Medium-term effects

Table 2. Target and Actual Macronutrient Energy Distribution, Glycemic Index (GI), and Glycemic Load (GL)*

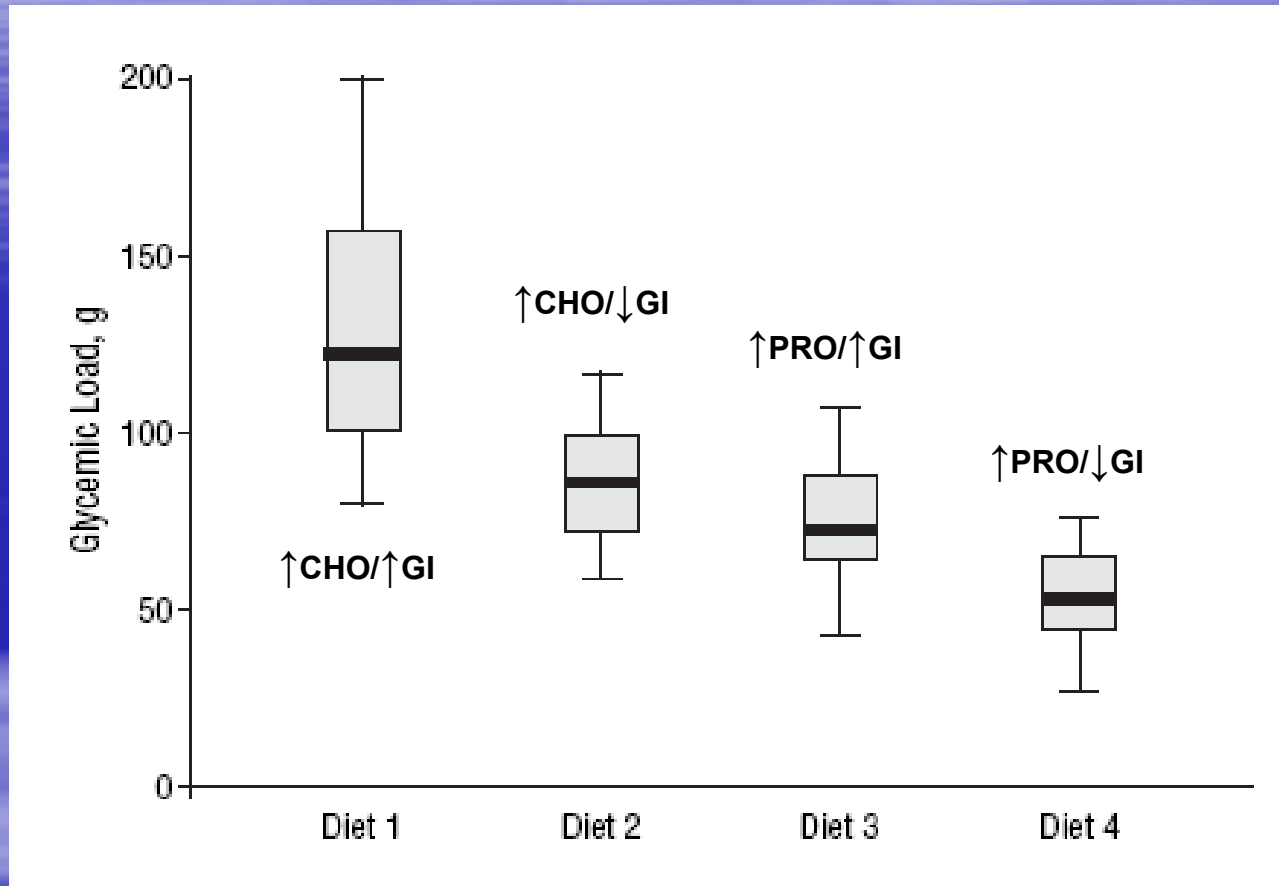
Variable	Diet 1		Diet 2		Diet 3		Diet 4		<i>P</i> Value†
	Target	Actual	Target	Actual	Target	Actual	Target	Actual	
CHO, % E	55	60 ± 1	55	56 ± 1	45	42 ± 1	45	40 ± 2	<.001
Protein, % E	15	18 ± 1	15	19 ± 0	25	28 ± 1	25	26 ± 1	<.001
Fat, % E	30	19 ± 1	30	22 ± 1	30	27 ± 1	30	29 ± 1	<.001
Alcohol, % E	0	2 ± 1	0	3 ± 1	0	2 ± 1	0	3 ± 1	.81
GI	67	70 ± 1	40	45 ± 1	57	59 ± 1	34	44 ± 1	<.001
GL, g	127	129 ± 8	75	89 ± 5	87	75 ± 3	54	59 ± 4	<.001

Abbreviations: CHO, carbohydrate; % E, percentage of total energy intake.

*Diet 1, high-CHO/high-GI; diet 2, high-CHO/low-GI; diet 3, high-protein/high-GI; and diet 4, high-protein/low-GI. Target values were the calculated values from sample menus. Actual values, which are expressed as mean ± SE, were calculated from food diaries completed during weeks 4 and 8 of the intervention.

†*P* value for comparison of actual values among the 4 diets.

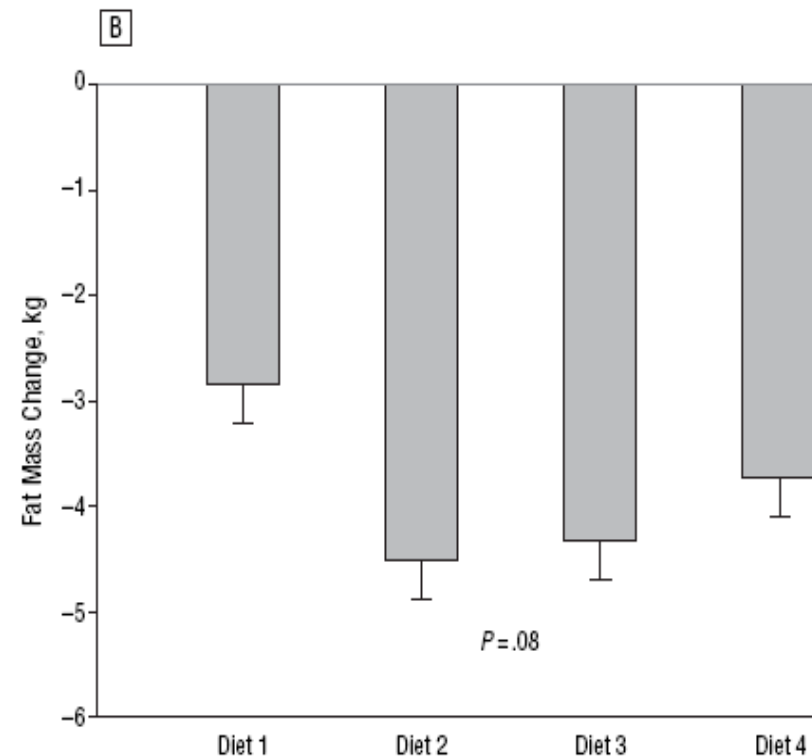
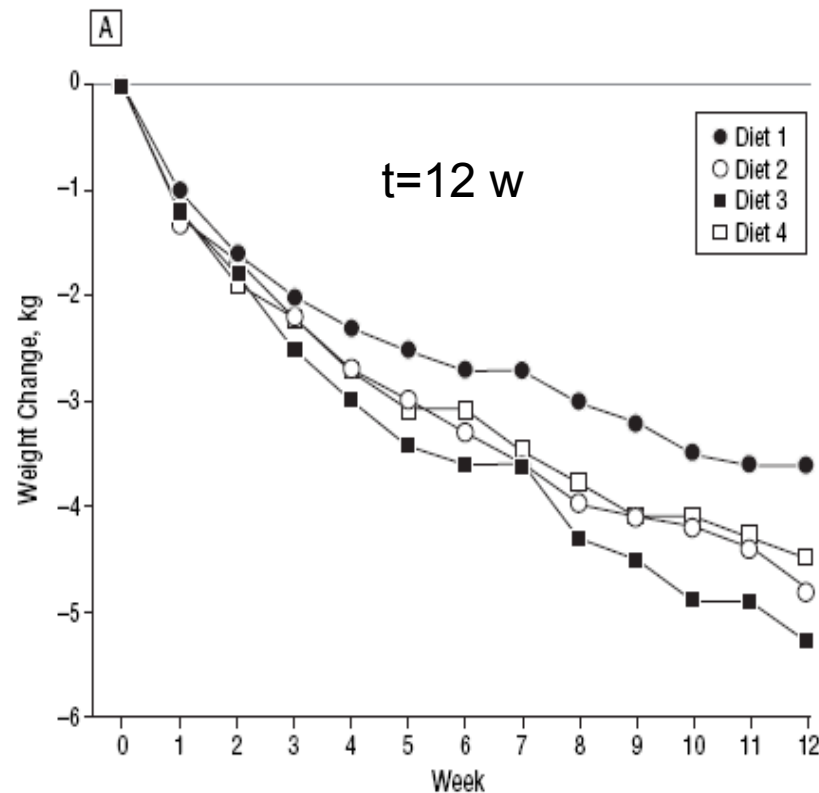
GI and Weight loss: Medium-term effects



Box plot of glycemic load of the 4 diets based on food diaries completed during weeks 4 and 8 of the intervention.

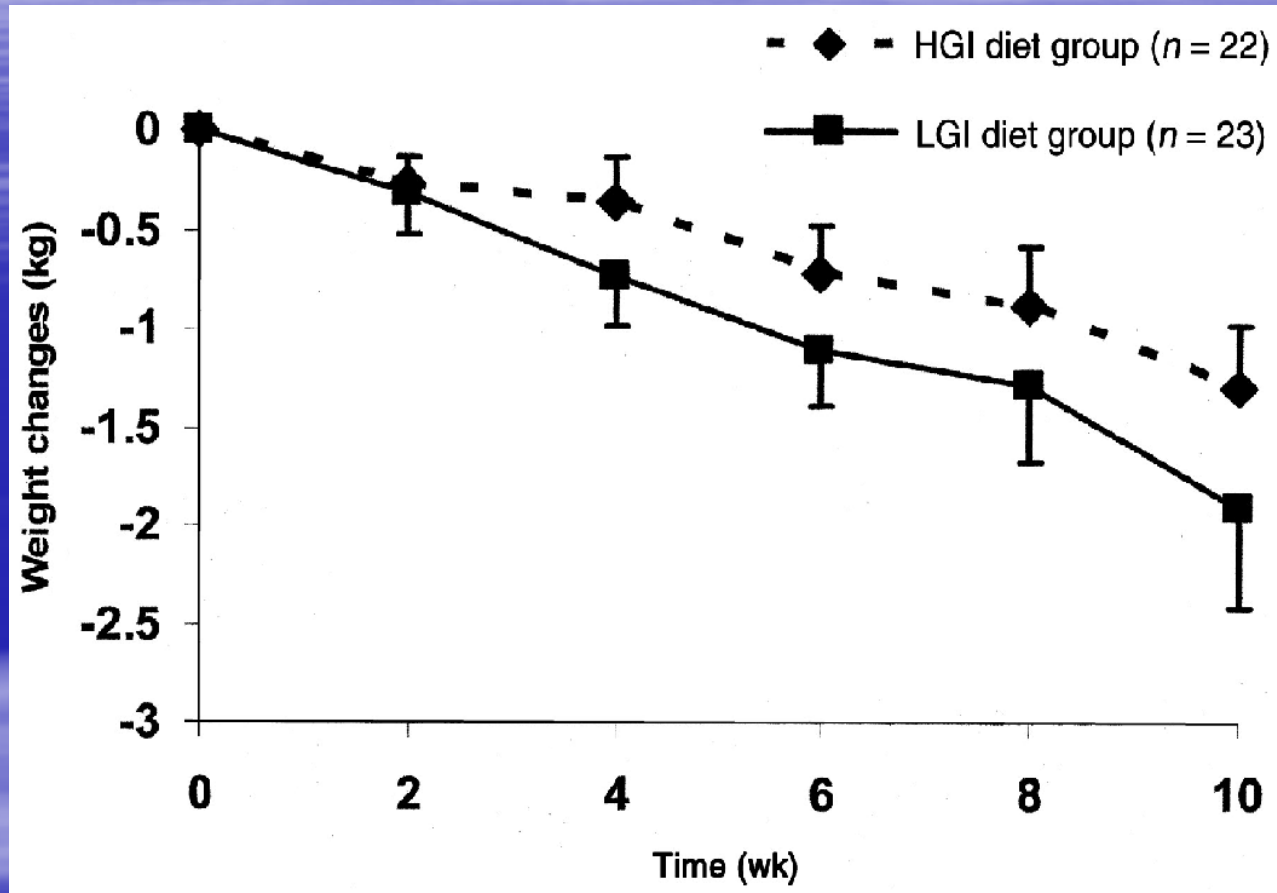
Mean dietary fiber intake was 25 g/d across all groups, but diet 2 was the only group to achieve the target intake (30 g/d; $P.001$).

GI and Weight loss: Medium-term effects



There were significant differences in the proportion of individuals who lost 5% or more of initial body weight: 31% of subjects on diet 1, 56% on diet 2, 66% on diet 3, and 33% on diet 4 ($P=.01$).

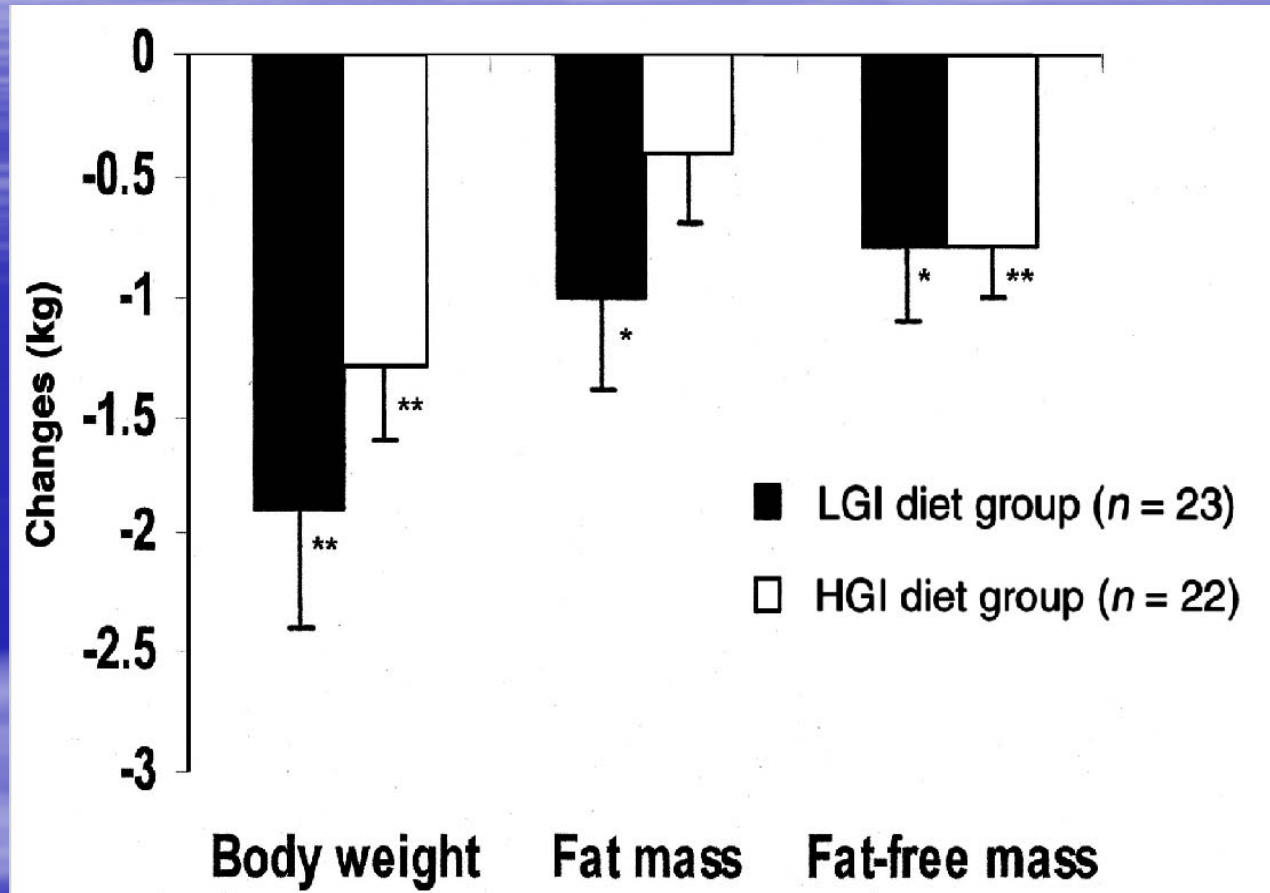
GI and Weight loss: Medium-term effects



Mean (\pm SEM) BW changes during 10 wk ad libitum intake of a HGI or a LGI diet in overweight women. diet, $P = 0.44$; time, $P = 0.001$.

There was no significant difference in BW changes between groups (LGI: -1.9 ± 0.5 kg; HGI: -1.3 ± 0.3 kg; $P = 0.31$), but body weight decreased significantly in both groups over time.

GI and Weight loss: Medium-term effects



BW and body-composition changes after 10 wk ad libitum intake of a HGI or a LGI diet in overweight women.

No significant differences in changes between groups were found
* $P < 0.05$, ** $P < 0.001$.

Medium-term Responses to HGI- and LGI Foods

- Greater decrease of fasting and stimulated serum insulin with LGI diets
 - In a crossover study, serum insulin levels dropped significantly, whereas C-peptide levels remained stable indicating greater hepatic clearance of insulin with LGI. Only after 12 mo of continued weight loss and maintenance of that loss, there was a significant drop in insulin production with LGI.
 - Hypertrophic β -cells in obesity
- LGI-diets may improve plasma lipid profile and fat mass
 - Tendency to decrease fasting plasma total and LDL-cholesterol and increase HDL-cholesterol
 - Dietary fibers bind cholesterol and may have an influence on plasma lipid profile
 - Tendency to decreased postprandial triacylglycerol excursion

Slabber M et al Am J Clin Nutr. 1994 Jul;60(1):48-53

Wee et al Med Sci Sports Exerc. 1999 Mar;31(3):393-9

Boivin A et al Am J Physiol. 1994 Oct;267(4 Pt 1):E620-7

Medium-term Responses to HGI- and LGI Foods

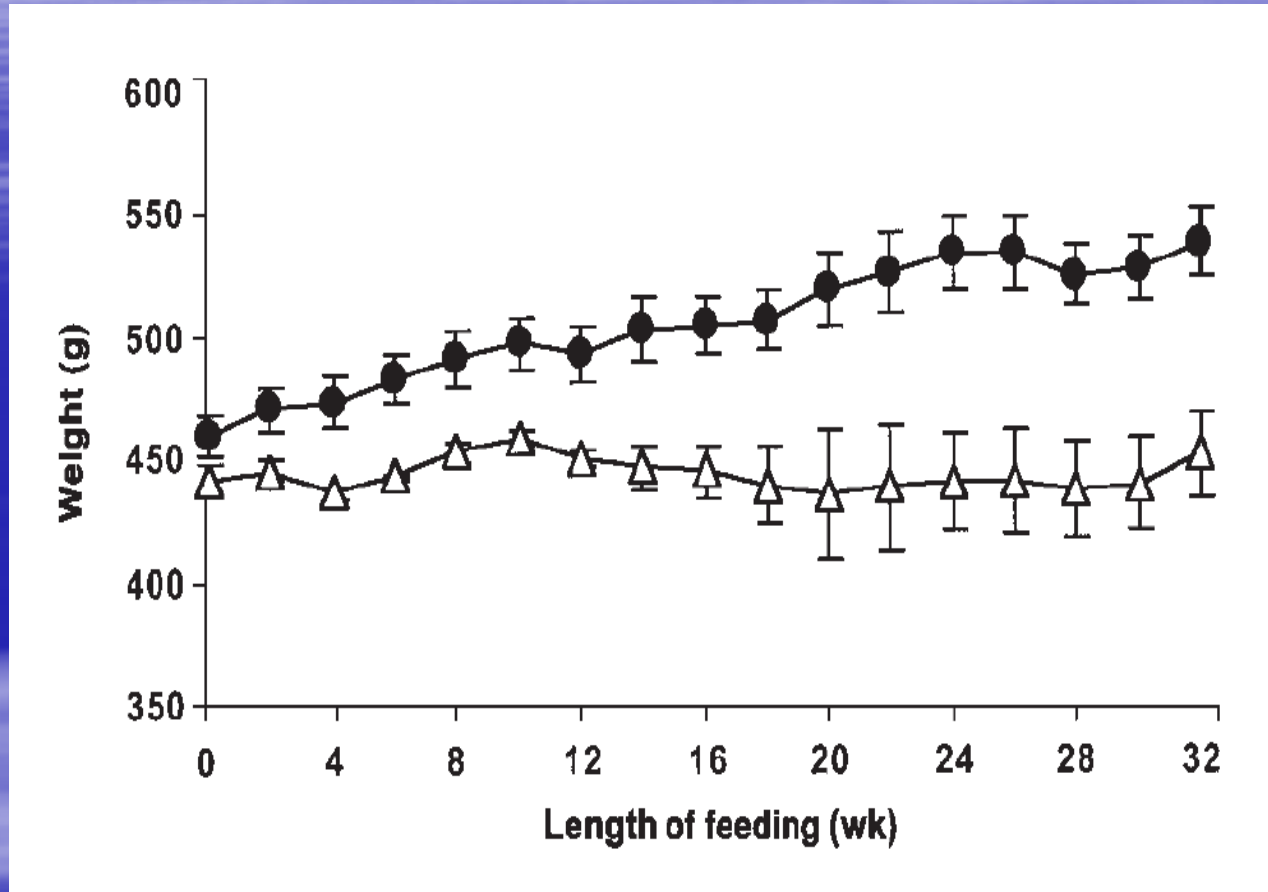
- LGI-diets may change body composition
 - Reduction of visceral fat pads
 - Difference in nitrogen balance and protein metabolism
 - Shift in substrate utilization
 - after an LGI test meal, carbohydrate oxidation was 12% lower and fat oxidation was 118% higher than after an HGI test meal
 - some proteins and genes specific to adipose tissue might be active in the regulation of fat mass by LGI diets
 - the LPL level in adipose tissue is positively correlated with insulinemia
- A diet's glycemic effect influences fuel storage within the body
 - chronic consumption of high-GI diets, compared with nutrient-balanced low-GI diets, was associated with higher muscle glycogen (14%) and muscle triacylglycerol (22%) concentrations
 - Chronic hyperinsulinemia?
 - HGI meals result in an increased glycogen storage in muscle cells if eaten within in the first 24 hours after prolonged exercise
 - Activation of glycogen synthase by insulin
 - Immediate availability of HGI starches

Kiens B, Richter EA Am J Clin Nutr. 1996 Jan;63(1):47-53

Burke LM et al Appl Physiol. 1993 Aug;75(2):1019-23

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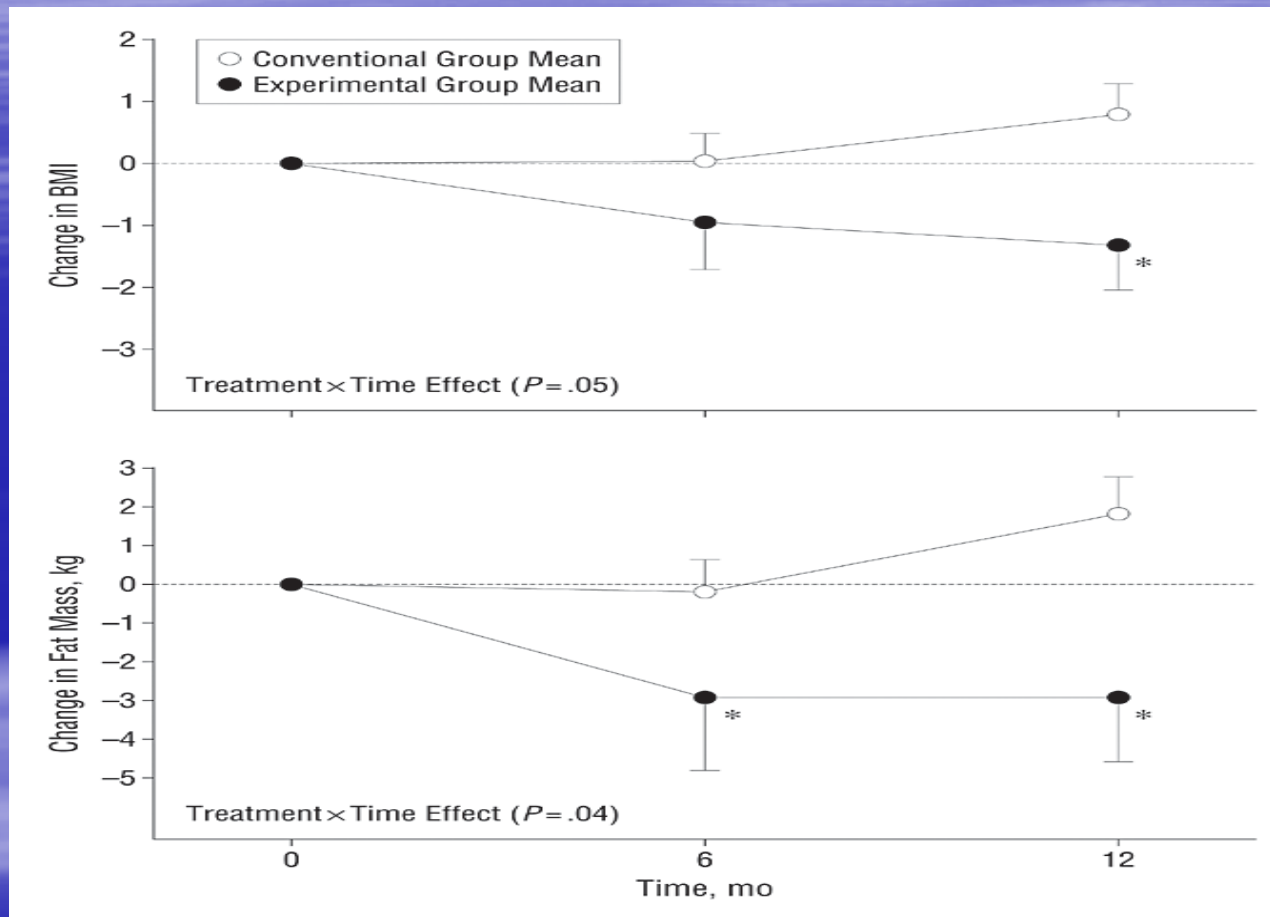
GI and Weight loss: Long-term effects



Weight changes in adult rats fed isoenergetic, nutrientbalanced diets based on high-glycemic-index (●) or low-glycemic-index (Δ) starch for 32 wk.

Whereas the LGI group remained weightstable, the HGI group gradually gained weight and were 16% heavier at the end of the study.

GI and Weight loss: Long-term effects



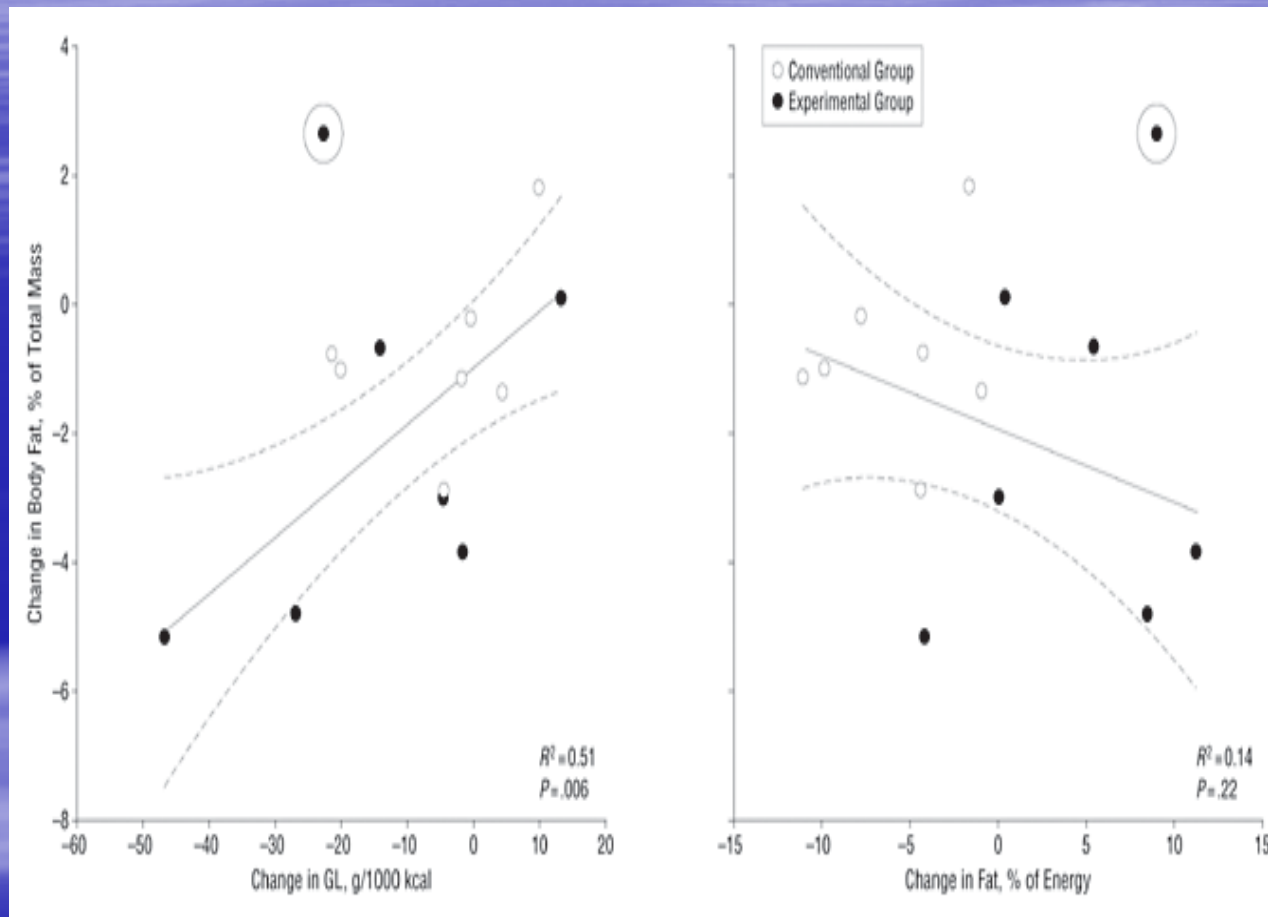
Changes over time for study outcomes. asterisk, $P < .05$.

BMI ($P = .03$) and fat mass ($P = .02$) decreased in the experimental group from 0 to 12 months, and neither outcome changed significantly in the conventional group.

Ebbeling, C. B. et al. Arch Pediatr Adolesc Med 2003;157:773-779.

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GI and Weight loss: Long-term effects



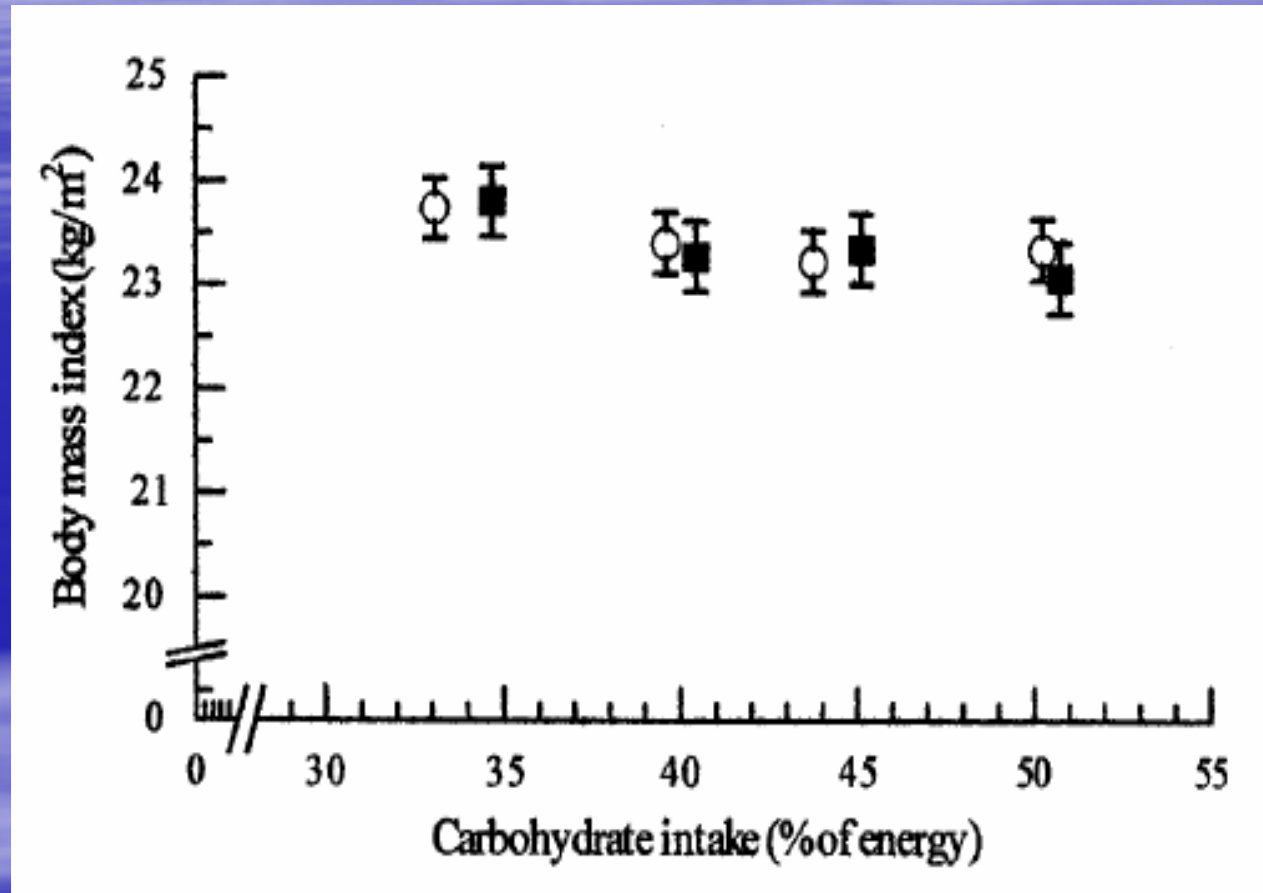
Changes in dietary glycemic load (GL) or fat intake as predictors of change in body fat. Note: Low GL diet was ad lib whereas low fat diet was energy restricted.

Change in GL was a strong predictor of this study outcome, explaining about half of the variance in both groups combined ($R^2 = 0.51$; $P = .006$).

Ebbeling, C. B. et al. Arch Pediatr Adolesc Med 2003;157:773-779.

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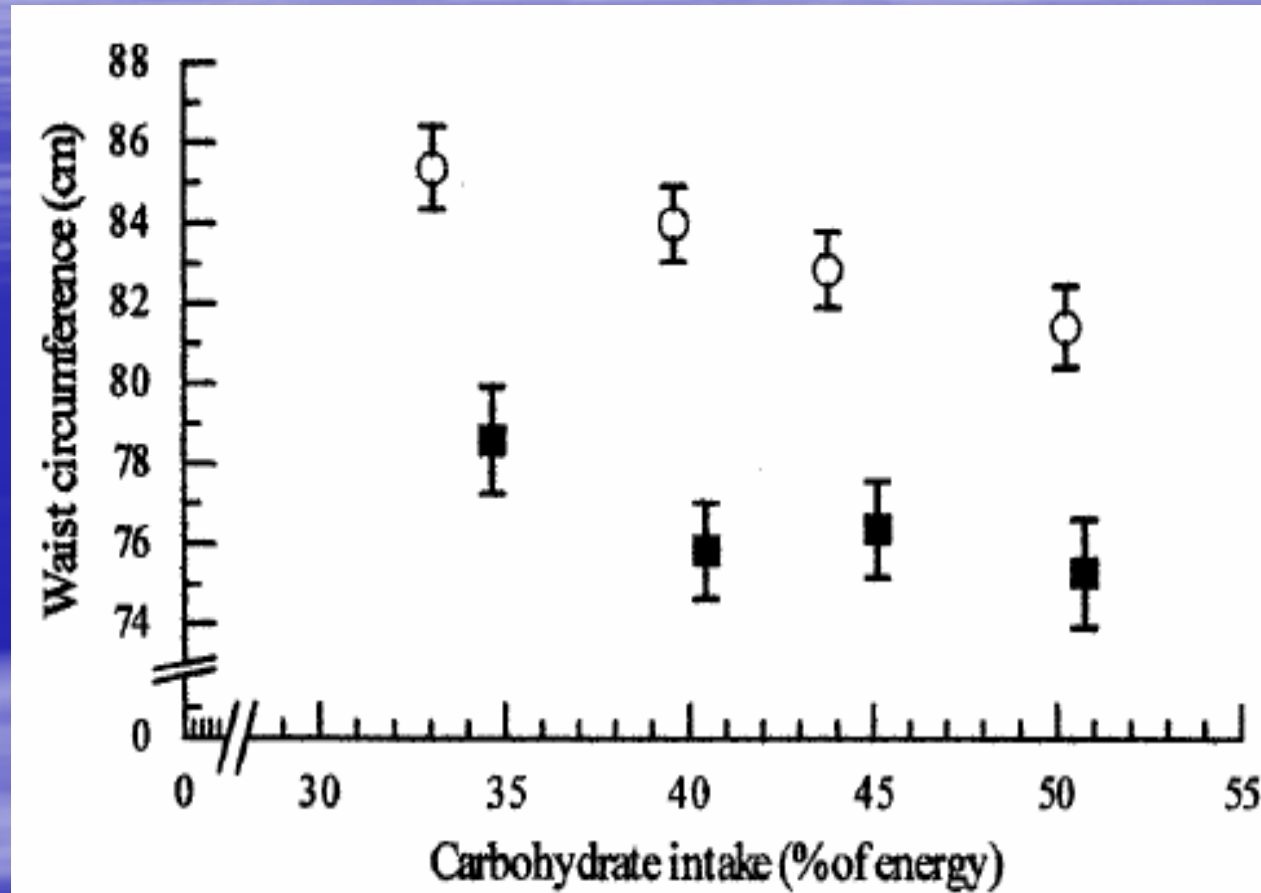
GI and Weight loss: Epidemiologic Evidence



Adjusted mean BMI (95% CI) in quartiles of carbohydrate intake (percentage of energy) for 1043 males (○) and 1006 females (■) with type 1 diabetes.

In both men and women, higher intakes of carbohydrates were associated with a lower BMI.

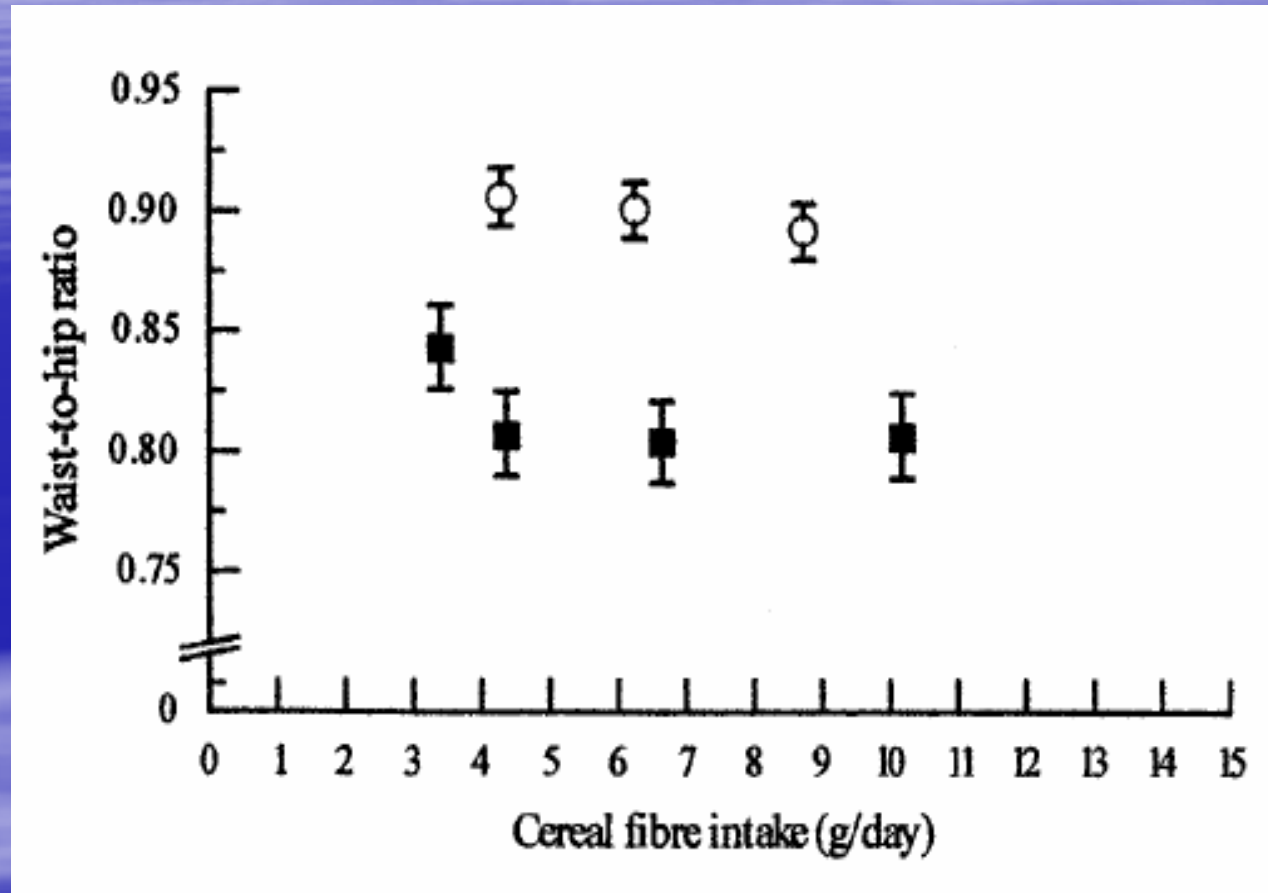
GI and Weight loss: Epidemiologic Evidence



Adjusted mean BMI (95% CI) in quartiles of carbohydrate intake (percentage of energy) for 1043 males (○) and 1006 females (■) with type 1 diabetes.

In both men and women, higher intakes of carbohydrates were associated with a lower WC.

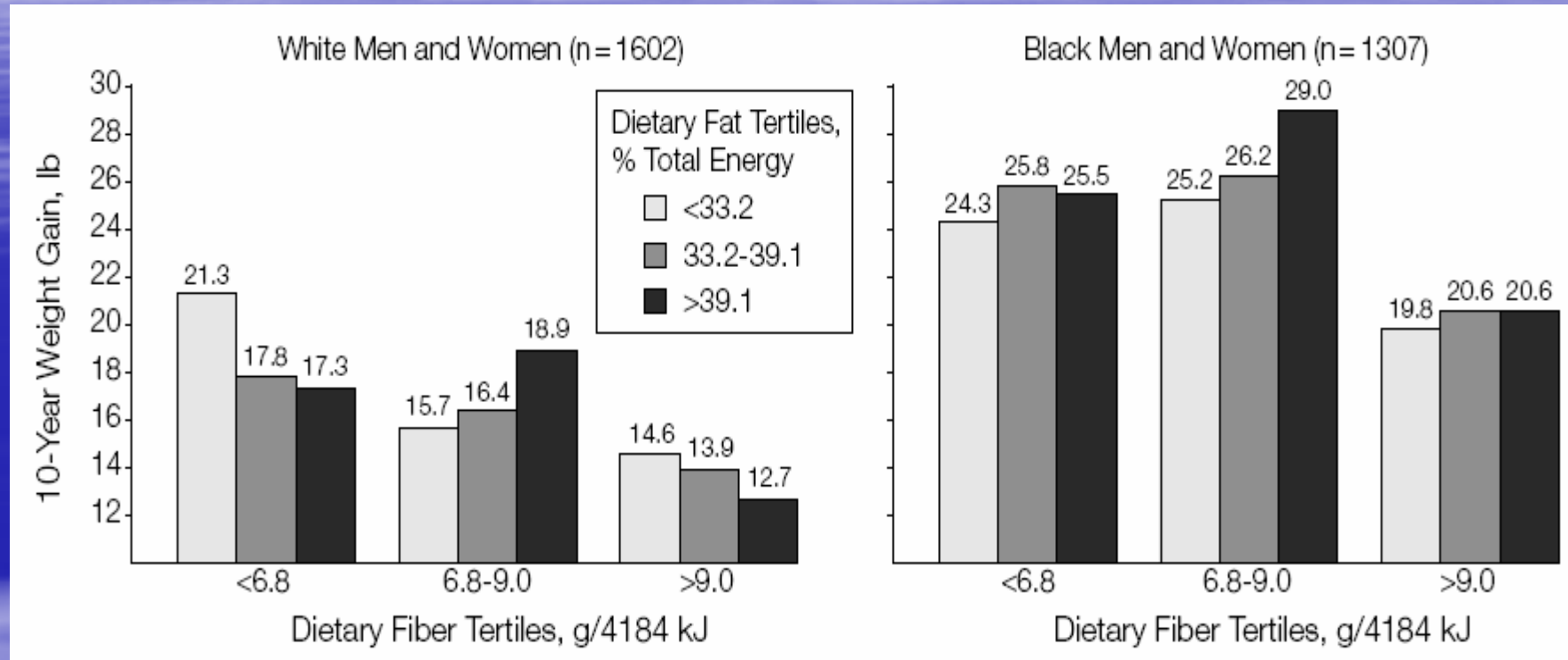
GI and Weight loss: Epidemiologic Evidence



Adjusted mean WHR (95% CI) in quartiles of cereal fibre intake (g/day) for 1043 males (○) and 1006 females (■) with type 1 diabetes.

In both men and women, an increased consumption of cereal fibre was related to a lower WHR.

GI and Weight loss: Epidemiologic Evidence



In the CARDIA study of young adults, low fiber consumption (GI was not assessed) predicted higher 10-y weight gain, waist-to-hip ratio, and 2-h postglucose insulin concentrations (a measure of insulin resistance) to a greater extent than did total or saturated fat consumption.

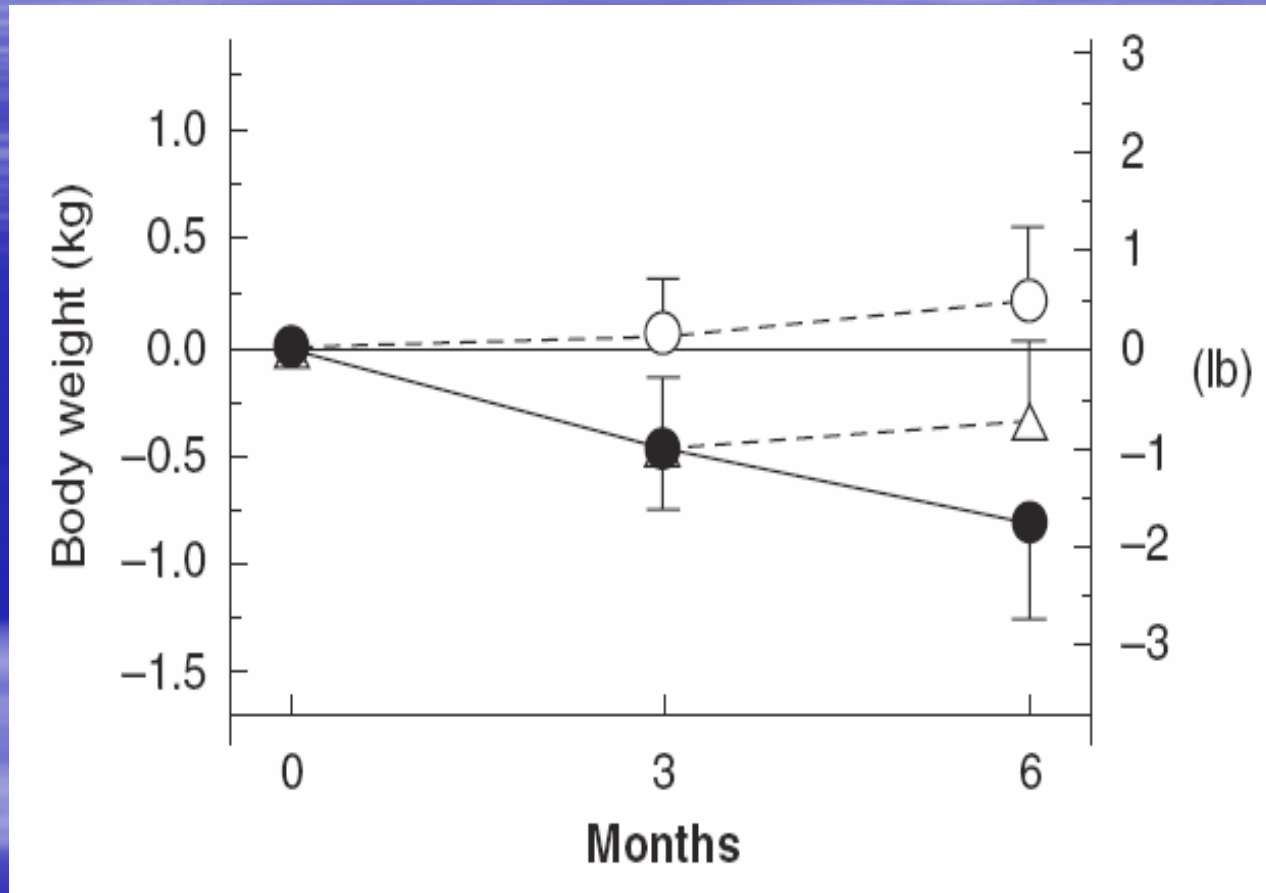
Ludwig, D. S. et al. JAMA 1999;282:1539-1546

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A hypothetical Biochemical Scenario

- Consumption of a CHO, HGI diet results in recurrent postprandial hyperglycemia and hyperinsulinemia that is accentuated in sedentary persons who are overweight, insulinresistant, or both
 - Increased carbohydrate oxidation and decreased fat oxidation throughout the postprandial period, whether the person is at rest or exercising
 - The expression of enzymes involved in lipid synthesis is up-regulated, whereas the expression of those involved in lipid oxidation are down-regulated.
- Counterregulatory hormonal responses (eg, of cortisol and noradrenaline) are higher with HGI foods because of the hyperglycemic-hypoglycemic rebound after consumption
 - Stimulation of gluconeogenesis from gluconeogenic amino acids as well as meal initiation in free-feeding individuals. The 0–6-h period following consumption of a high-GI diet is therefore characterized by a greater dependence on carbohydrate and protein as sources of fuel and less dependence on fat. Because carbohydrate and protein stores are limited, their higher rate of usage may stimulate appetite and encourage overconsumption.
 - Small energy imbalances that are characteristic of modern lifestyles are more likely to promote gradual expansion of the fat stores (possibly at the expense of lean tissue) when the diet is based on high-GI foods.

Should obese patients be counselled to follow a low-glycaemic index diet?

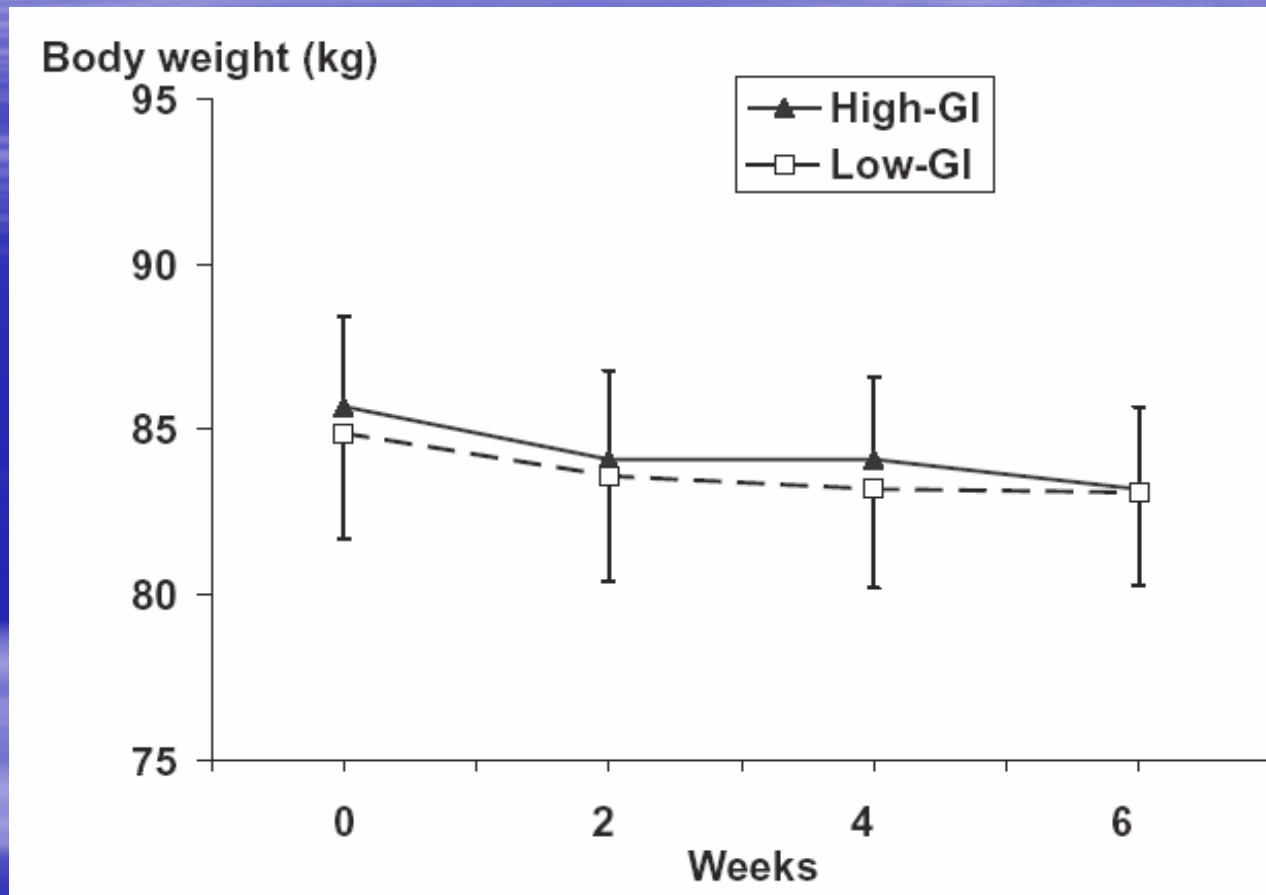


Body weight changes (mean \pm SEM) in diabetic subjects after three and six months of treatment with carbohydrate from breakfast cereals with a high GI (●), a low GI (○) or with monounsaturated fatty acids (Δ). There were no differences between diets.

Tsihlias EB et al Am J Clin Nutr. 2000 Aug;72(2):439-49

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Should obese patients be counselled to follow a low-glycaemic index diet?

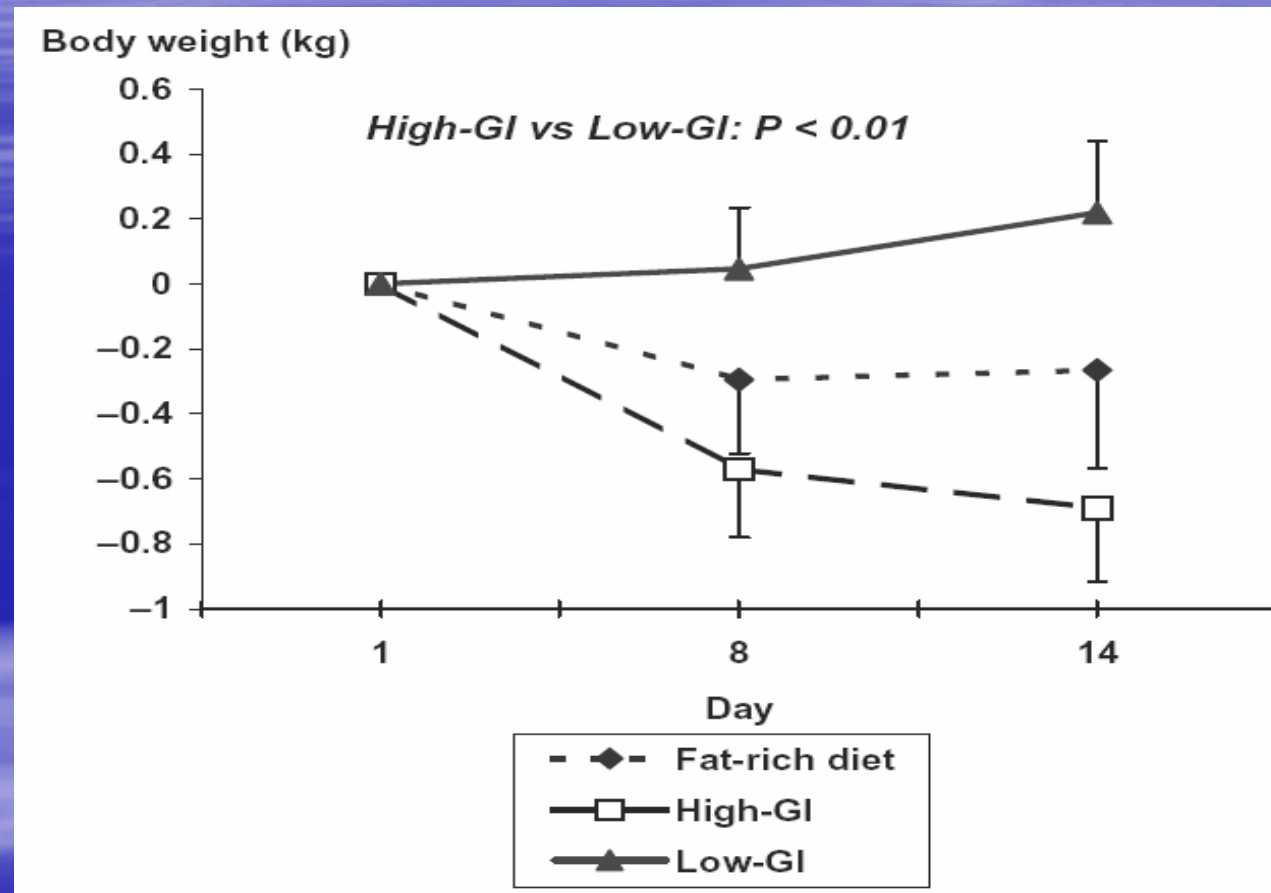


Body weight (mean \pm SEM) in six patients with non-insulin-dependent diabetes mellitus during six weeks on energy-restricted diets with either a high or a low glycaemic index. There were no differences between diets.

Wolever TM et al Diabetes Care. 1992 Apr;15(4):562-4

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Should obese patients be counselled to follow a low-glycaemic index diet?



Body weight changes (mean \pm SEM) in 20 normal-weight women after 14 days of *ad libitum* intake of a HGI (starch-rich), LGI (sucrose-rich) or high-fat diet. $P < 0.05$, analysis of variance, diet effect. $P < 0.01$, HGI vs. LGI.

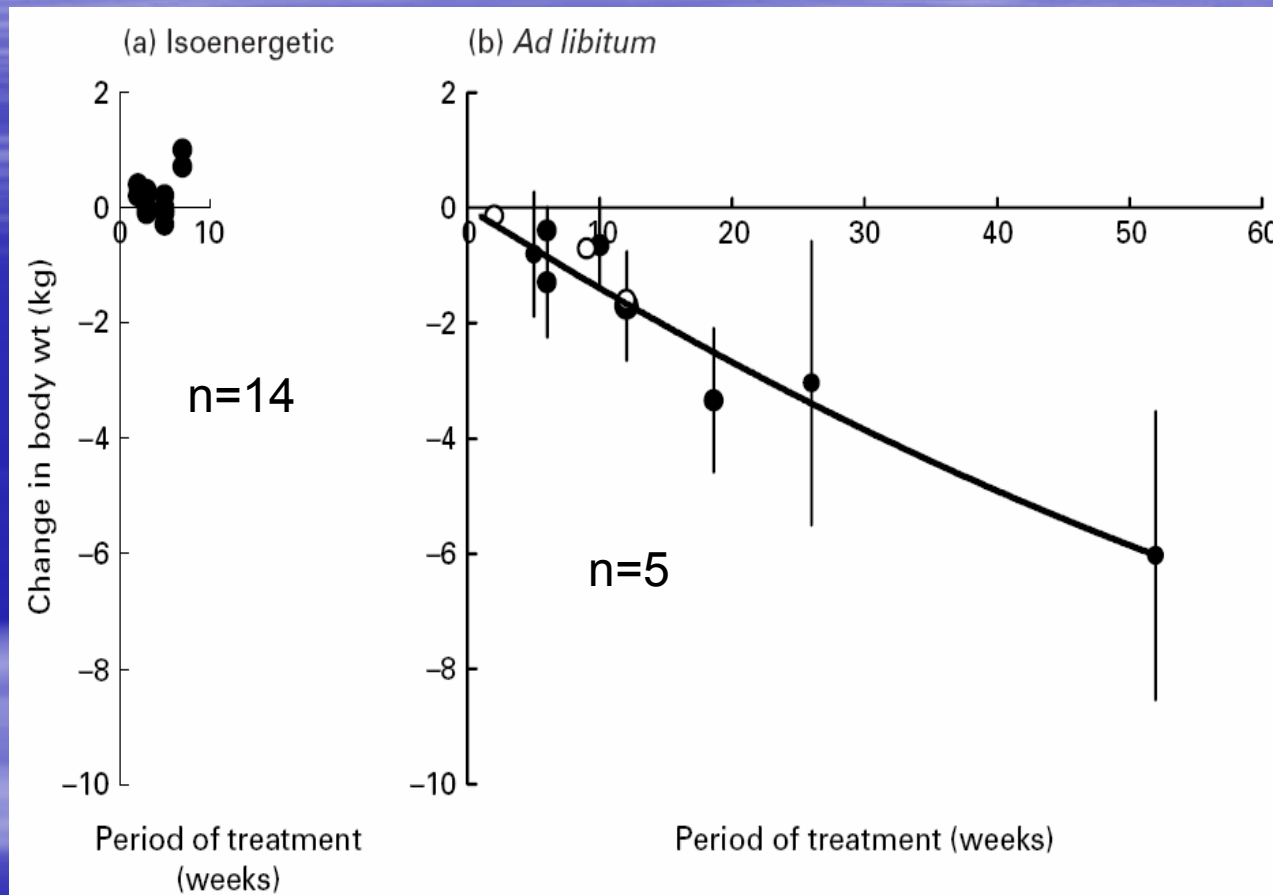
Should obese patients be counselled to follow a low-glycaemic index diet? NO!

- The data from short-term human intervention studies does not provide convincing evidence that low-GI meals have a more positive effect on satiety, hunger and food intake than high-GI meals
 - The summary of 31 studies which measured hunger and/or satiety shows that a low-GI test meal was associated with greater satiety or reduced hunger in 15 studies, whereas there was no difference in 16 other studies
- 13 isoenergetic long-term studies reported a greater weight loss on a low-GI diet in two studies and a greater weight loss on a high-GI diet in one study. In 10 studies, however, no differences were observed
- Data from five studies using energy restricted diets showed that a LGI diet decreased body weight in two studies, whereas there were no differences in the remaining three studies
 - The mean weight loss was somewhat larger on LGI (4.8 kg) than on HGI (3.3 kg) diets, which might indicate a possible benefit of LGI diets

Should obese patients be counselled to follow a low-glycaemic index diet? No.

- A total of 70 human intervention studies were examined to clarify the role of GI in body weight regulation. No clear pattern was observed. Based on the available evidence, it is therefore still advisable to recommend a low-fat diet with increased amounts of carbohydrate or protein and increased dietary fiber content. The type of carbohydrate – including GI or saccharide structure (simple, complex) – seems of less importance

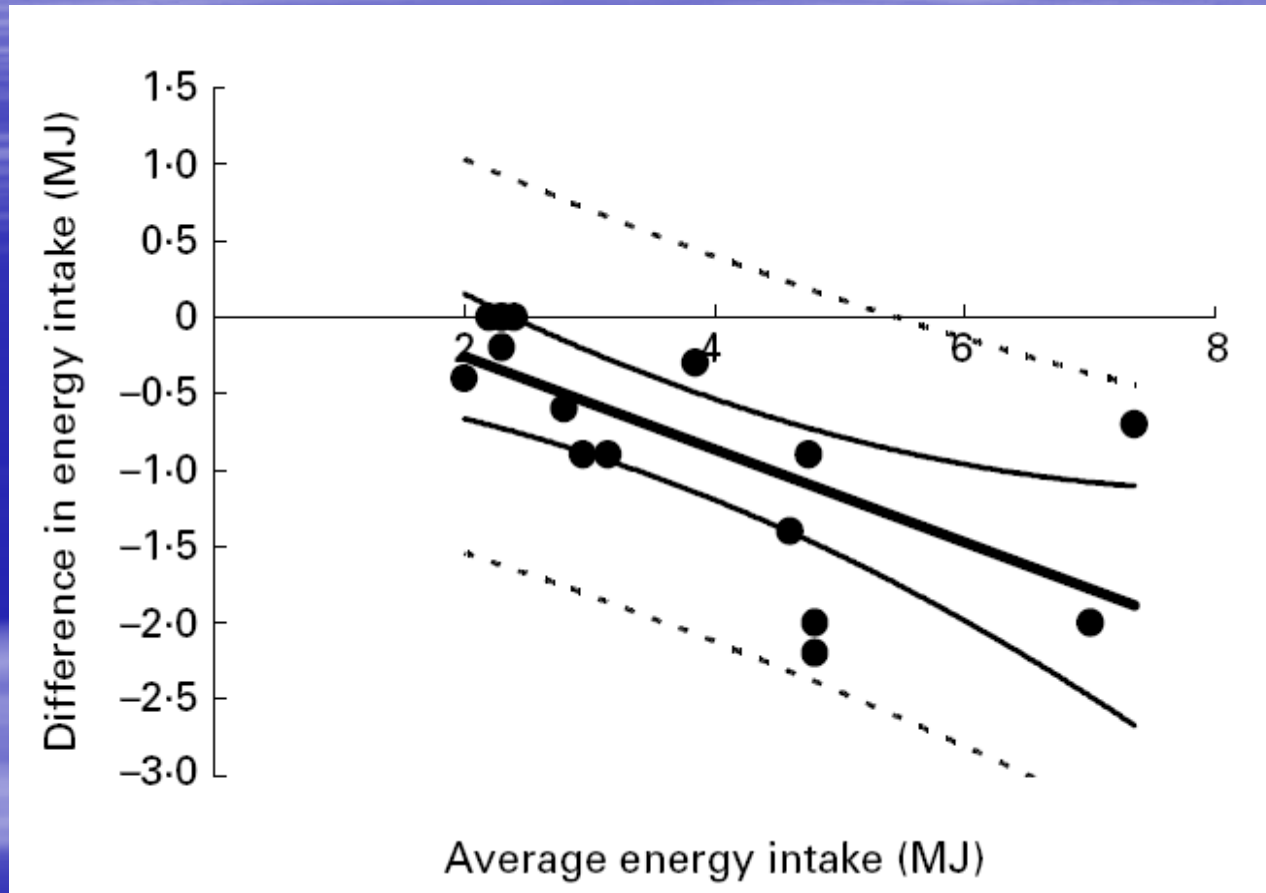
Should obese patients be counselled to follow a low-glycaemic index diet?



Glycaemic load and body weight: The isoenergetic comparisons comprise fourteen studies. The ad libitum comparison comprised five studies.

Data available by verified extraction from reliable studies with mostly adequate dietary information clearly indicate that LGI vs. HGI diets eaten *ad libitum* result in a lower body weight.

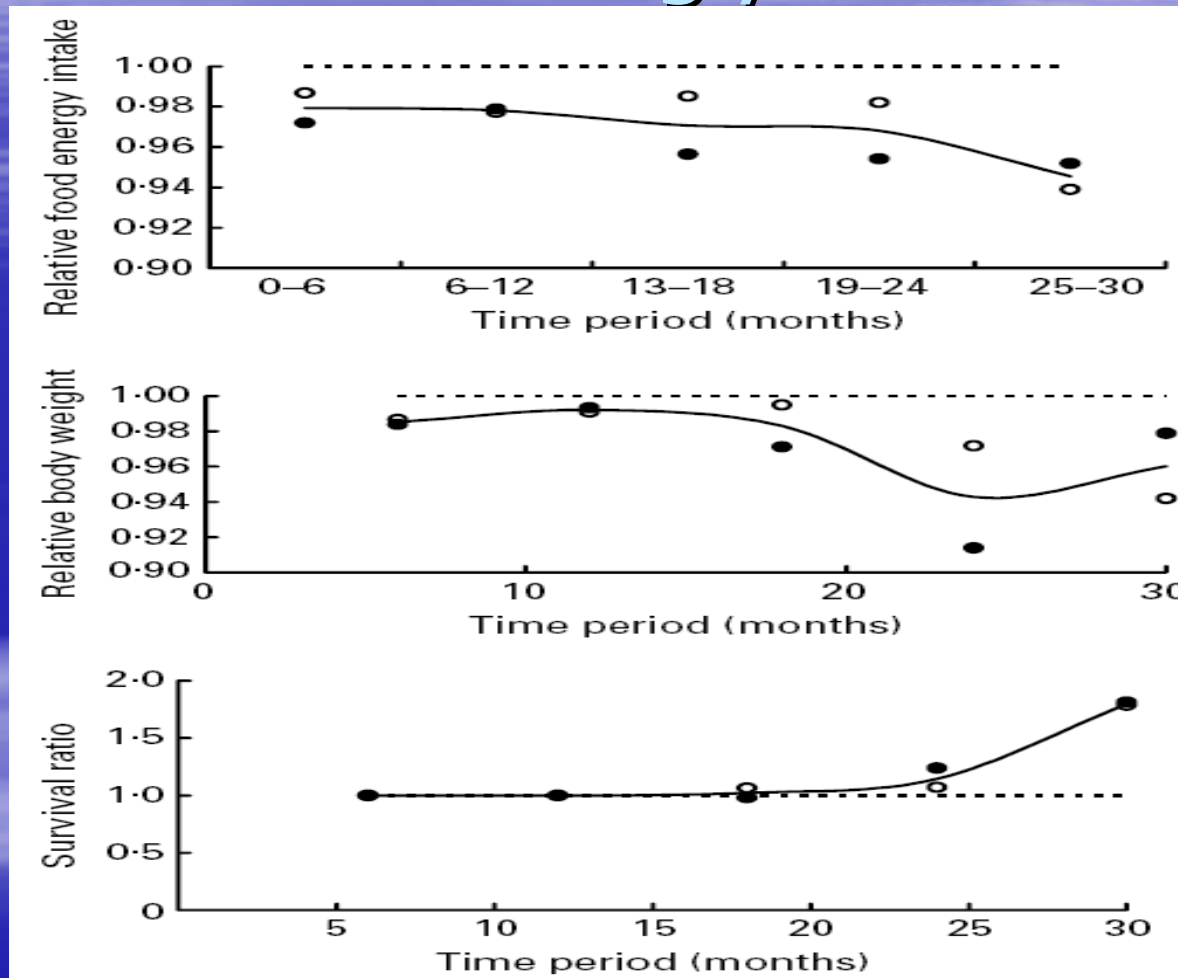
Should obese patients be counselled to follow a low-glycaemic index diet?



Energy intake in human subjects on reducing the glycaemic load (GL) of a previous meal.

There appears to be little effect on cumulative energy intake up to about 2000 MJ, but at higher cumulative intakes during the day there appears to be a substantial and significant reduction in energy intake (slope $P < 0.05$) over the duration of these data (range 2 h–2 d).

Should obese patients be counselled to follow a low-glycaemic index diet?



Energy intake, body weight and survival in animals consuming a diet of reduced glycaemic load fed *ad libitum*.

● = male rats
○ = female rats

Should obese patients be counselled to follow a low-glycaemic index diet? YES!

- Weight loss on energy-restricted, reduced-fat diets may be increased when such diets are modified to lower GI
- When energy intake is not restricted, low GI and/or glycaemic load diets may produce greater weight loss than conventional, low-fat diets
- A low GI diet may, in addition, modulate the rate of weight gain during physiological states of increased nutrient storage, such as pregnancy
 - Lower intra-pregnancy weight gain with a LGI diet (11.8 vs. 19.7 kg, $P < 0.01$)
- Reduction in GI or glycaemic load would be predicted to have beneficial effects on rates of lipid oxidation and preservation of lean body tissue

Should obese patients be counselled to follow a low-glycaemic index diet? YES!

- The metabolic profile associated with consumption of low GI diets may foster satiety and reduce food intake
 - *ad libitum* energy consumption is strongly predicted by the plasma blood glucose nadir
 - Reduction in GI by addition of soluble fibre has been shown to lower hunger ratings and the desire to eat for as long as 13 h after the meal and to promote longer-term negative energy balance
- Epidemiological data suggest that low glycaemic load diets may confer substantial ($\approx 50\%$) protection against CVD in overweight women (by lowering triglycerides and raising HDL cholesterol concentrations)
- A preliminary meta-analysis of all 13 published interventional studies suggested a beneficial effect of low GI diets on the level of serum lipids

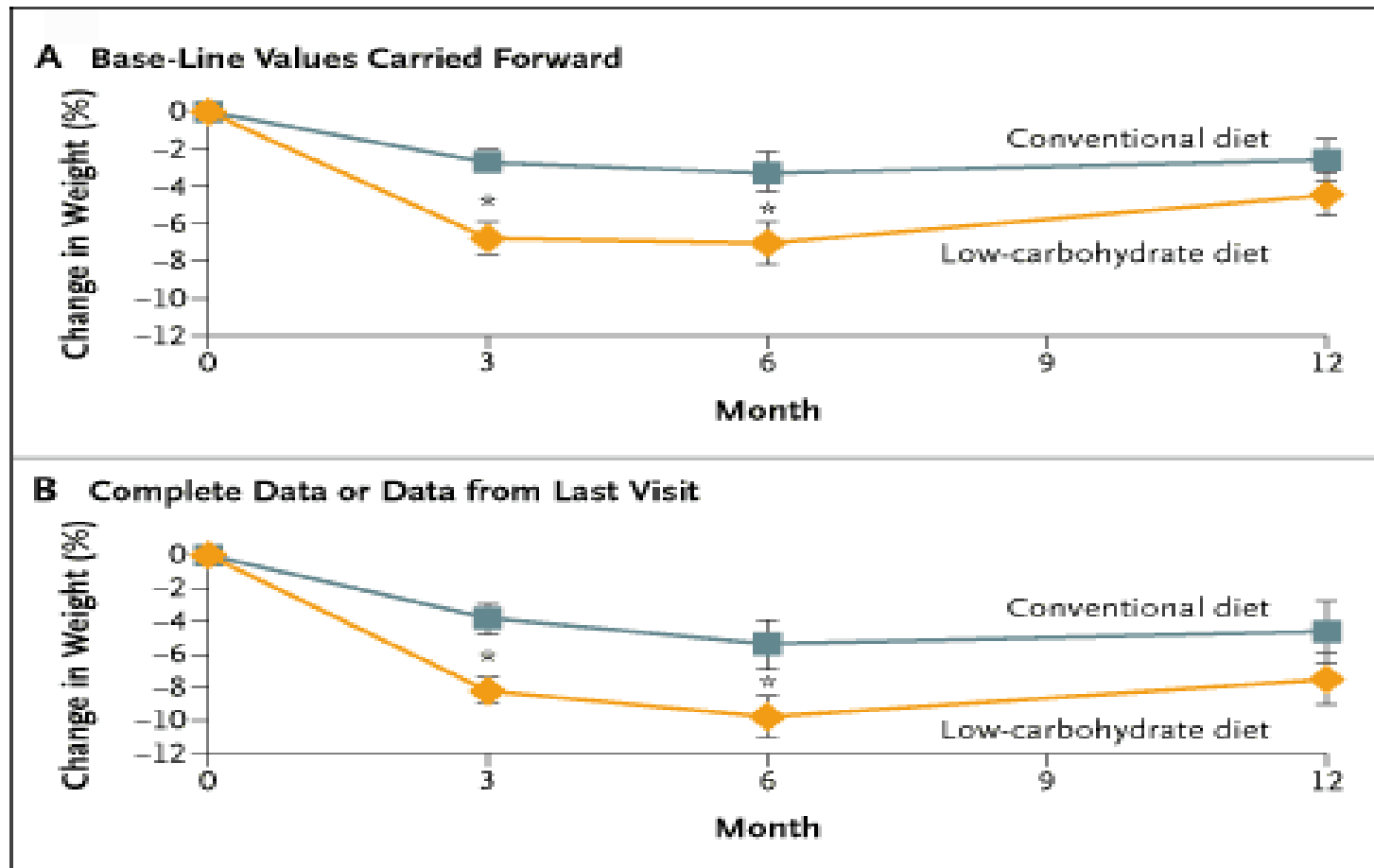
Should obese patients be counselled to follow a low-glycaemic index diet? YES!

- LGI diets might decrease risk for type 2 diabetes, independent of weight change, by reducing demand on the pancreatic b cell in the postprandial period and also by decreasing insulin resistance
 - lower average 24-hour blood glucose levels
 - lower average 24-hour insulin levels
 - lower C-peptide excretion
- LGI diets lead to lower glycated hemoglobin (HbA1c) concentrations in nondiabetic and diabetic individuals
 - An increase of 1% in HbA(1c) is associated with a 28% ($P<0.002$) increase in risk of death independent of age, blood pressure, serum cholesterol, body mass index, and cigarette smoking habit

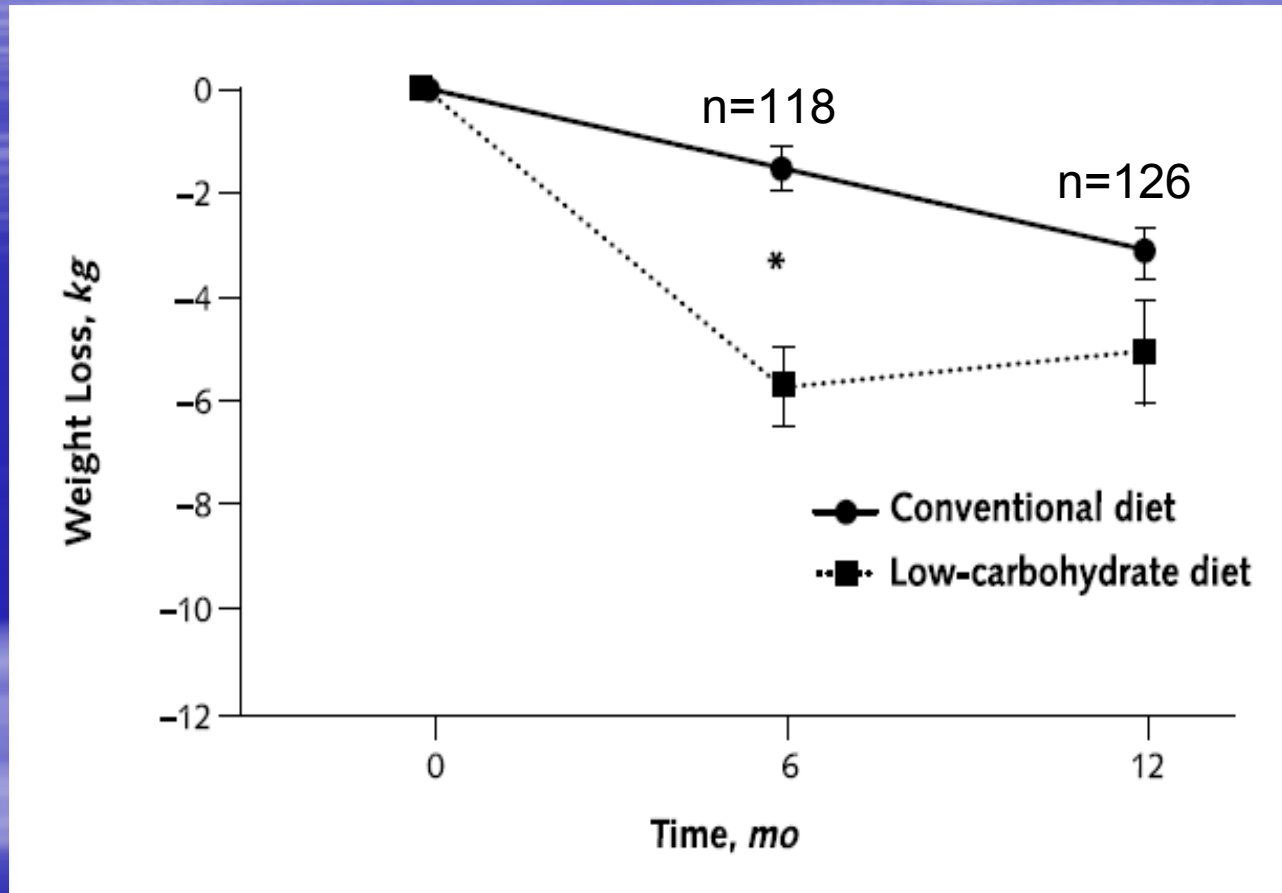
Jenkins DJ, et al. Am J Clin Nutr. 1987 Dec;46(6):968-75
Miller JC Am J Clin Nutr. 1994 Mar;59(3 Suppl):747S-752S
Livesey G Nutr Res Rev. 2003 38:117-121
Khaw KT et al BMJ. 2001 Jan 6;322(7277):15-8

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Comparison of Weight Loss between a Conventional and a low-COH Diet



Comparison of Weight Loss between a Conventional and a low-COH Diet



*** P 0.003 for comparisons between diet groups by random-coefficient analysis. The difference in weight loss was not significant between the 2 diet groups by 1 year (P 0.195 before and P 0.2 after adjustment for baseline variables, by random-coefficient analysis).**

Comparison of different diets with respect to compliance

Mean Self-reported Dietary Adherence Scores of All 4 Diet Groups, According to Study Month

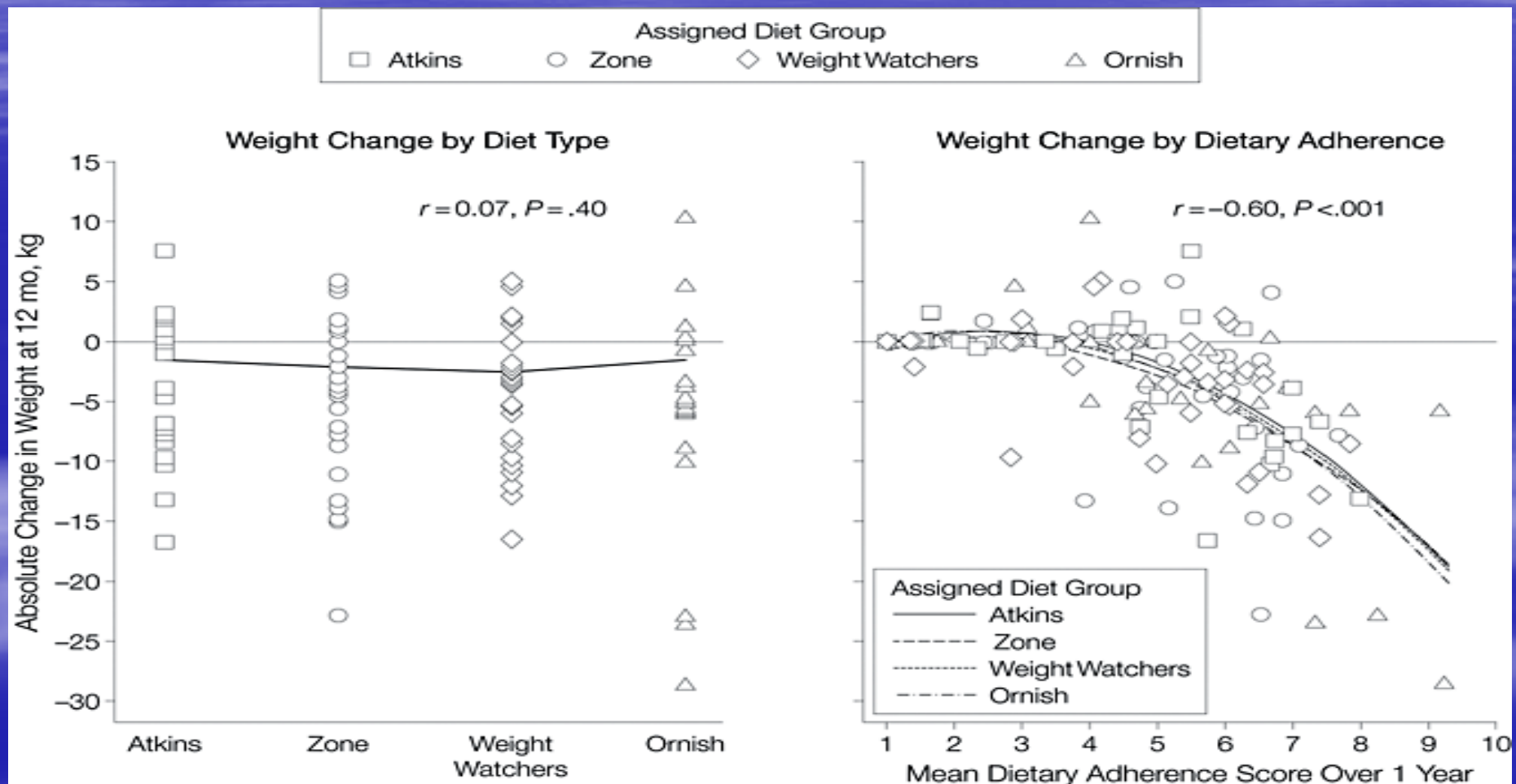


Dansinger ML et al. JAMA. 2005 Jan 5;293(1):43-53

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Comparison of different diets with respect to weight loss

One-Year Changes in Body Weight as a Function of Diet Group and Dietary Adherence Level for All Study Participants



Conclusion

- Poor sustainability and adherence rates results in modest weight loss and cardiac risk factor independent of diet type. Cardiac risk factor reductions is associated with weight loss regardless of diet type, underscoring the concept that adherence level rather than diet type is the key determinant of clinical benefits.
- General recommendation of a low GI in the treatment and prevention of overweight and obesity is still premature, although the preponderance of evidence suggests that low GI diets may be effective in the treatment of obesity and prevention of type 2 diabetes and CVD.

Montignac

Myth or Reality?

Thank you for your
attention



swissestetix

THE BEAUTY DOCTORS

The Greek Ideal

Dietary factor	Recommended dietary intake ranges (as a share of total energy intake)
Total fat	15–30%
Polyunsaturated fatty acids	6–10%
Saturated fatty acids	<10%
<i>Trans</i> fatty acids	<1%
Total carbohydrate*	55–75%
Free sugars†	<10%
Protein‡	10–15%
Cholesterol	<300 mg
Sodium chloride (sodium)	<5 g (<2 g)
Fruit and vegetables	>400 g
Total dietary fibre/non-starch polysaccharides	>25 g/20 g from whole-grain cereals, fruit and vegetables

Source: Adapted from the World Health Organization (WHO)/Food and Agriculture Organization (FAO) report *Diet, Nutrition and The Prevention of Chronic Diseases*¹, Table 6, p. 56.
 *Percentage of total energy available after taking into account that consumed as protein and fat; hence the wide range.
 †The term 'free sugars' refers to all monosaccharides and disaccharides added to foods by the manufacturer, cook or consumer, plus sugars naturally present in honey, syrups and fruit juices.
 ‡The suggested range should be seen in the light of the Joint WHO/FAO/United Nations University Expert Consultation on Protein and Amino Acid Requirements in Human Nutrition, held in Geneva, 9–16 April 2002.

Source: World Health Organization (WHO)/Food and Agriculture Organization (FAO) (2003) *Diet, Nutrition and The Prevention of Chronic Diseases Report of a Joint WHO/FAO Expert Consultation*. WHO Technical Report Series No. 916 Geneva WHO

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Public Health Nutr. 2006 Aug;9(5):584-95. Links

The changing structure of diets in the European Union in relation to healthy eating guidelines.

[Schmidhuber J.](#)

[Traill WB.](#)

Food and Agriculture Organization, Rome, Italy.

OBJECTIVE: Our objective in this paper is to assess diets in the European Union (EU) in relation to the recommendations of the recent World Health Organization/Food and Agriculture Organization expert consultation and to show how diets have changed between 1961 and 2001. **DATA AND METHODS:** Computations make use of FAOSTAT data on food availability at country level linked to a food composition database to convert foods to nutrients. We further explore the growing similarity of diets in the EU by making use of a consumption similarity index. The index provides a single number measure of dietary overlap between countries. **RESULTS:** The data confirm the excessive consumption by almost all countries of saturated fats, cholesterol and sugars, and the convergence of nutrient intakes across the EU. Whereas in 1961 diets in several European countries were more similar to US diets than to those of other European countries, this is no longer the case; moreover, while EU diets have become more homogeneous, the EU as a whole and the USA have become less similar over time. **CONCLUSIONS:** Although the dominant cause of greater similarity in EU diets over the period studied is increased intakes in Mediterranean countries of saturated fats, cholesterol and sugar, also important are reductions in saturated fat and sugar in some Northern European countries. This suggests that healthy eating messages are finally having an impact on diets; a distinctly European diet may also be emerging.

PMID: 16923290 [PubMed - indexed for MEDLINE]

The real Picture

Nutrient/food item	Criterion	Number of countries meeting the recommendation in (3-year average):				
		1961–1963	1969–1971	1979–1981	1989–1991	1999–2001
Total protein	> 30%	0	1	1	1	1
	< 15%	0	0	0	0	0
Fat	> 30%	10	10	13	14	14
	< 15%	0	0	0	0	0
Saturated fatty acids	> 10%	9	10	11	13	12
Polyunsaturated fatty acids	< 6%	12	12	7	6	5
	> 10%	0	0	0	0	0
Carbohydrates	< 55%	8	12	13	14	14
	> 75%	0	0	0	0	0
Cholesterol	> 300 mg person ⁻¹ day ⁻¹	10	10	13	14	14
Fruits and vegetables	> 400 g person ⁻¹ day ⁻¹	6	9	9	12	14
Sugar	> 10%	8	11	10	9	10

* Maximum 14.

Number of countries that meet the recommendations in the European Union.
The results of a headcount (maximum number = 14)

Source: World Health Organization (WHO)/Food and Agriculture Organization (FAO) (2003) Diet, Nutrition and The Prevention of Chronic Diseases Report of a Joint WHO/FAO Expert Consultation. WHO Technical Report Series No. 916
Geneva WHO

Dr. C.P. Davis

Public Health Nutr. 2006 Aug;9(5):584-95. Links

The changing structure of diets in the European Union in relation to healthy eating guidelines.

[Schmidhuber J.](#)

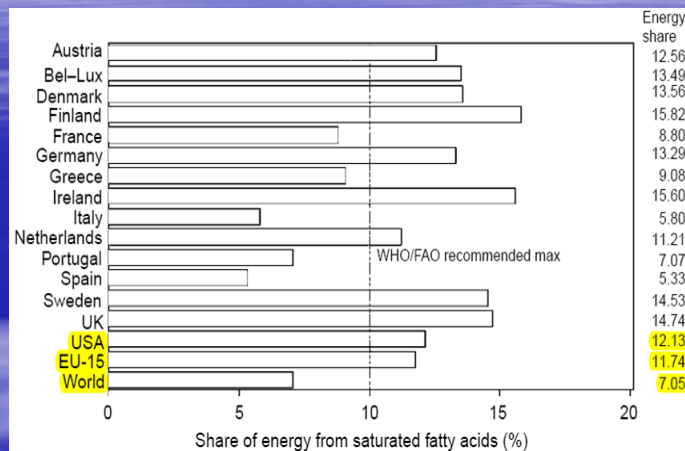
[Traill WB.](#)

Food and Agriculture Organization, Rome, Italy.

OBJECTIVE: Our objective in this paper is to assess diets in the European Union (EU) in relation to the recommendations of the recent World Health Organization/Food and Agriculture Organization expert consultation and to show how diets have changed between 1961 and 2001. **DATA AND METHODS:** Computations make use of FAOSTAT data on food availability at country level linked to a food composition database to convert foods to nutrients. We further explore the growing similarity of diets in the EU by making use of a consumption similarity index. The index provides a single number measure of dietary overlap between countries. **RESULTS:** The data confirm the excessive consumption by almost all countries of saturated fats, cholesterol and sugars, and the convergence of nutrient intakes across the EU. Whereas in 1961 diets in several European countries were more similar to US diets than to those of other European countries, this is no longer the case; moreover, while EU diets have become more homogeneous, the EU as a whole and the USA have become less similar over time. **CONCLUSIONS:** Although the dominant cause of greater similarity in EU diets over the period studied is increased intakes in Mediterranean countries of saturated fats, cholesterol and sugar, also important are reductions in saturated fat and sugar in some Northern European countries. This suggests that healthy eating messages are finally having an impact on diets; a distinctly European diet may also be emerging.

PMID: 16923290 [PubMed - indexed for MEDLINE]

The real Picture: Fat Consumption in 1961



Share of energy from saturated fatty acids versus World Health Organization (WHO)/Food and Agriculture Organization (FAO) recommendation, 1961.

Source: Josef Schmidhuber, Global Perspectives Studies Group, FAO (2003)

Dr. C.P. Davis

Public Health Nutr. 2006 Aug;9(5):584-95. Links

The changing structure of diets in the European Union in relation to healthy eating guidelines.

[Schmidhuber J.](#)

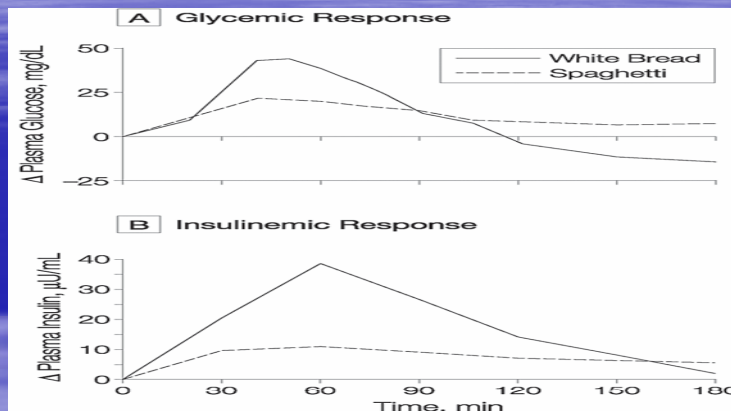
[Traill WB.](#)

Food and Agriculture Organization, Rome, Italy.

OBJECTIVE: Our objective in this paper is to assess diets in the European Union (EU) in relation to the recommendations of the recent World Health Organization/Food and Agriculture Organization expert consultation and to show how diets have changed between 1961 and 2001. **DATA AND METHODS:** Computations make use of FAOSTAT data on food availability at country level linked to a food composition database to convert foods to nutrients. We further explore the growing similarity of diets in the EU by making use of a consumption similarity index. The index provides a single number measure of dietary overlap between countries. **RESULTS:** The data confirm the excessive consumption by almost all countries of saturated fats, cholesterol and sugars, and the convergence of nutrient intakes across the EU. Whereas in 1961 diets in several European countries were more similar to US diets than to those of other European countries, this is no longer the case; moreover, while EU diets have become more homogeneous, the EU as a whole and the USA have become less similar over time. **CONCLUSIONS:** Although the dominant cause of greater similarity in EU diets over the period studied is increased intakes in Mediterranean countries of saturated fats, cholesterol and sugar, also important are reductions in saturated fat and sugar in some Northern European countries. This suggests that healthy eating messages are finally having an impact on diets; a distinctly European diet may also be emerging.

PMID: 16923290 [PubMed - indexed for MEDLINE]

Glycemic and Insulinemic Responses After Ingestion of Carbohydrates



Responses were measured after ingestion of 50 g of CHD as white bread or spaghetti made from the identical ingredients

Ludwig, D. S. JAMA 2002;287:2414-2423.

Dr. C.P. Davis

JAMA. 2002 May 8;287(18):2414-23. [Links](#)

Comment in:

[JAMA. 2002 Aug 14;288\(6\):695; author reply 695.](#)

The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease.

[Ludwig DS.](#)

Department of Medicine, Children's Hospital, 300 Longwood Ave, Boston, MA 02115, USA.
david.ludwig@tch.harvard.edu

The glycemic index was proposed in 1981 as an alternative system for classifying carbohydrate-containing food. Since then, several hundred scientific articles and numerous popular diet books have been published on the topic. However, the clinical significance of the glycemic index remains the subject of debate. The purpose of this review is to examine the physiological effects of the glycemic index and the relevance of these effects in preventing and treating obesity, diabetes, and cardiovascular disease.

PMID: 11988062 [PubMed - indexed for MEDLINE]

Glycemic Index and Glycemic Load: Values of Representative Foods

Food	Glycemic Index†	Glycemic Load‡
Instant rice	91	24.8 (110 g)
Baked potato	85	20.3 (110 g)
Corn flakes	84	21.0 (225 mL)
Carrot	71	3.8 (55 g)
White bread	70	21.0 (2 slices)
Rye bread	65	19.5 (2 slices)
Muesli	56	16.8 (110 mL)
Banana	53	13.3 (170 g)
Spaghetti	41	16.4 (55 g)
Apple	36	8.1 (170 g)
Lentil beans	29	5.7 (110 mL)
Milk	27	3.2 (225 mL)
Peanuts	14	0.7 (30 g)
Broccoli

Glycemic load is calculated as the glycemic index multiplied by grams of COH per serving size, indicated in parentheses, divided by 100%.

Ludwig, D. S. JAMA 2002;287:2414-2423.

Dr. C.P. Davis

JAMA. 2002 May 8;287(18):2414-23. Links

Comment in:

[JAMA. 2002 Aug 14;288\(6\):695; author reply 695.](#)

The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease.

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Department of Medicine, Children's Hospital, 300 Longwood Ave, Boston, MA 02115, USA.
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PMID: 11988062 [PubMed - indexed for MEDLINE]

Glycemic Index and Glycemic Load: Is the Concept Valid?

The assumed glycemic index (GI) and carbohydrate (CHO) content used to calculate the weight of food portions tested in Study 1¹

Food	GI (glucose = 100)	CHO g/100 g	CHO content of portion tested g	Weight of portion tested g
White bread ²	70	44	15	34
Porridge ³	41	61	25	41
Dried apricots	31	48	34	76
Apple ⁴	36	12	30	247
Grain bread ⁵	31	29	34	118
Ice cream ⁶	50	31	21	68
Lentils ⁷	26	29	40	138
Sweet corn ⁸	55	19	19	100
All-Bran ⁹	42	45	26	58
Rice Bubbles ¹⁰	81	87	13	15
Basmati rice ¹¹	58	64	18	28

All portions had the same dietary glycemic load as one slice of white bread.

Brand-Miller JC et al J Nutr. 2003 Sep;133(9):2728-32

Dr. C.P. Davis

J Nutr. 2003 Sep;133(9):2728-32. Links

Comment in:

[J Nutr. 2003 Sep;133\(9\):2695-6.](#)

Physiological validation of the concept of glycemic load in lean young adults.

[Brand-Miller JC](#),

[Thomas M](#),

[Swan V](#),

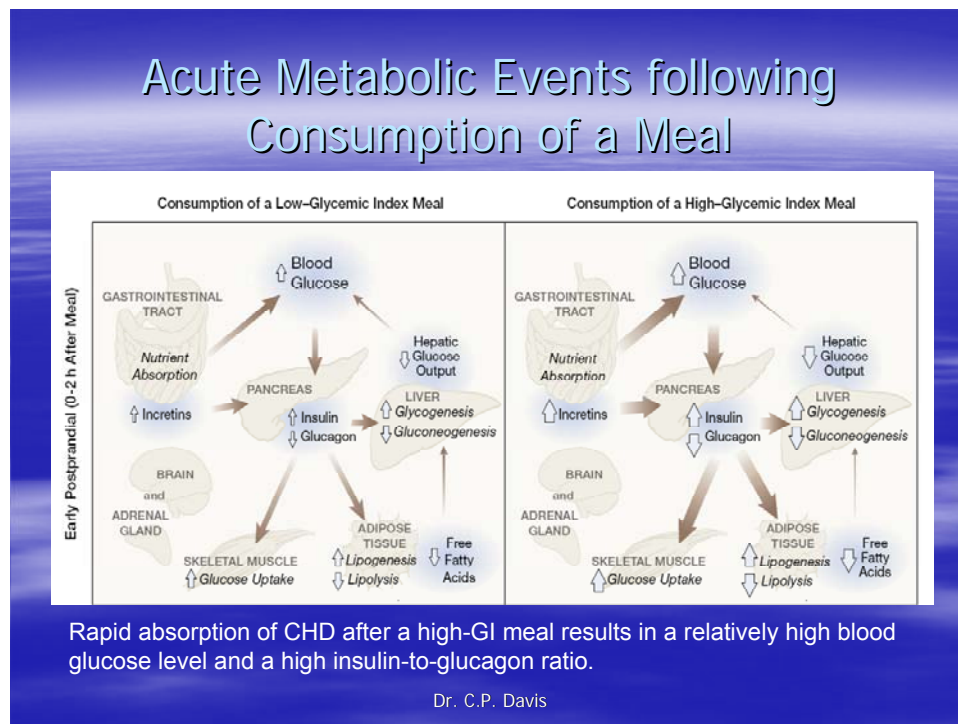
[Ahmad ZI](#),

[Petocz P](#),

[Colagiuri S](#).

Human Nutrition Unit, School of Molecular and Microbial Biosciences, University of Sydney, Sydney, NSW, Australia. j.brandmiller@staff.usyd.edu.au

Dietary glycemic load, the mathematical product of the glycemic index (GI) of a food and its carbohydrate content, has been proposed as an indicator of the glucose response and insulin demand induced by a serving of food. To validate this concept in vivo, we tested the hypotheses that 1). portions of different foods with the same glycemic load produce similar glycemic responses; and 2). stepwise increases in glycemic load for a range of foods produce proportional increases in glycemia and insulinemia. In the first study, 10 healthy subjects consumed 10 different foods in random order in amounts calculated to have the same glycemic load as one slice of white bread. Capillary blood samples were taken at regular intervals over the next 2 h. The glycemic response as determined by area under the curve was not different from that of white bread for nine foods. However, lentils produced lower than predicted responses ($P < 0.05$). In the second study, another group of subjects was tested to determine the effects of increasing glycemic load using a balanced 5 x 5 Greco-Latin square design balanced for four variables: subject, dose, food and order. Two sets of five foods were consumed at five different glycemic loads (doses) equivalent to one, two, three, four and six slices of bread. Stepwise increases in glycemic load produced significant and predictable increases in both glycemia ($P < 0.001$) and insulinemia ($P < 0.001$). These findings support the concept of dietary glycemic load as a measure of overall glycemic response and insulin demand.



Incretins: glucagon-like peptide-1 and glucose-dependant insulinotropic polypeptide

JAMA. 2002 May 8;287(18):2414-23. Links

Comment in:

JAMA. 2002 Aug 14;288(6):695; author reply 695.

The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease.

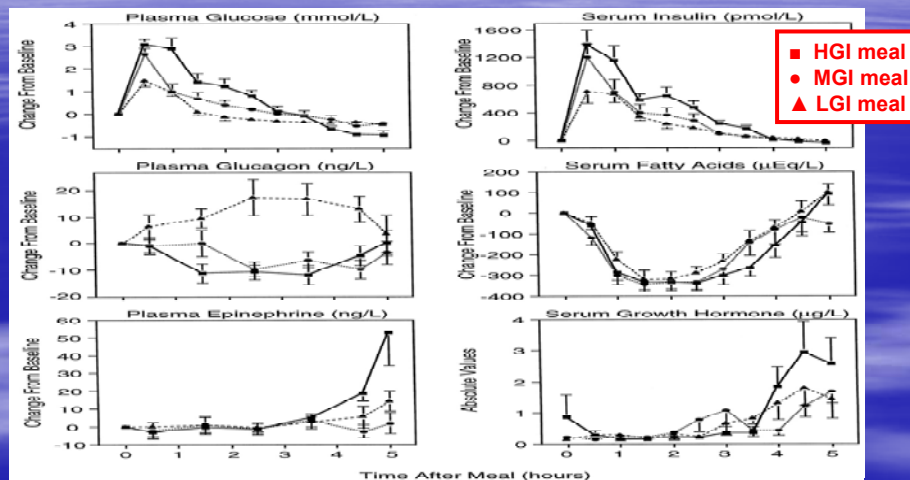
Ludwig DS.

Department of Medicine, Children's Hospital, 300 Longwood Ave, Boston, MA 02115, USA.
david.ludwig@tch.harvard.edu

The glycemic index was proposed in 1981 as an alternative system for classifying carbohydrate-containing food. Since then, several hundred scientific articles and numerous popular diet books have been published on the topic. However, the clinical significance of the glycemic index remains the subject of debate. The purpose of this review is to examine the physiological effects of the glycemic index and the relevance of these effects in preventing and treating obesity, diabetes, and cardiovascular disease.

PMID: 11988062 [PubMed - indexed for MEDLINE]

Hormonal and Metabolic Changes after test Breakfasts



Ludwig DS et al. Pediatrics. 1999 Mar;103(3):E26

Dr. C.P. Davis

Pediatrics. 1999 Mar;103(3):E26. Links

High glycemic index foods, overeating, and obesity.

[Ludwig DS,](#)

[Majzoub JA,](#)

[Al-Zahrani A,](#)

[Dallal GE,](#)

[Blanco I,](#)

[Roberts SB.](#)

Division of Endocrinology, Department of Medicine, Children's Hospital, Boston, 300 Longwood Ave, Boston, MA 02115, USA.

OBJECTIVE: The prevalence of obesity has increased dramatically in recent years. However, the role of dietary composition in body weight regulation remains unclear. The purpose of this work was to investigate the acute effects of dietary glycemic index (GI) on energy metabolism and voluntary food intake in obese subjects. **METHODS:** Twelve obese teenage boys were evaluated on three separate occasions using a crossover study protocol. During each evaluation, subjects consumed identical test meals at breakfast and lunch that had a low, medium, or high GI. The high- and medium-GI meals were designed to have similar macronutrient composition, fiber content, and palatability, and all meals for each subject had equal energy content. After breakfast, plasma and serum concentrations of metabolic fuels and hormones were measured. Ad libitum food intake was determined in the 5-hour period after lunch. **RESULTS:** Voluntary energy intake after the high-GI meal (5.8 megajoule [mJ]) was 53% greater than after the medium-GI meal (3.8 mJ), and 81% greater than after the low-GI meal (3.2 mJ). In addition, compared with the low-GI meal, the high-GI meal resulted in higher serum insulin levels, lower plasma glucagon levels, lower postabsorptive plasma glucose and serum fatty acids levels, and elevation in plasma epinephrine. The area under the glycemic response curve for each test meal accounted for 53% of the variance in food intake within subjects. **CONCLUSIONS:** The rapid absorption of glucose after consumption of high-GI meals induces a sequence of hormonal and metabolic changes that promote excessive food intake in obese subjects. Additional studies are needed to examine the relationship between dietary GI and long-term body weight regulation.

High-GI Foods = Obesity?

- No long-term clinical trials examining the effects of dietary GI on BW regulation
- Kabir M et al: rats fed amylopectin (HGI starch) compared with amylose (LGI starch) for 3-5 weeks exhibited larger adipocyte diameter, increased glucose incorporation into lipids, and greater fatty acid synthase
- Pawlak DB et al: animals fed a high-GI diet for 7 weeks developed increased epididymal fat mass
- Pawlak DB et al: animals fed a high-GI diet for 32 weeks developed marked obesity

Kabir M et al J Nutr. 1998 Jan;128(1):35-43
Pawlak et al J Nutr. 2001 Jan;131(1):99-104.
Pawlak DB et al Obes Res. 2000; 8:128S

Dr. C.P. Davis

J Nutr. 1998 Jan;128(1):35-43. [Links](#)

Dietary amylose-amylopectin starch content affects glucose and lipid metabolism in adipocytes of normal and diabetic rats.

[Kabir M](#),
[Rizkalla SW](#),
[Champ M](#),
[Luo J](#),
[Boillot J](#),
[Bruzzo F](#),
[Slama G](#).

Department of Diabetes, INSERM U341, University of Pierre et Marie Curie, Hotel-Dieu Hospital, 75004 Paris, France.

The aim of this study was to evaluate the effects of the chronic consumption of two starches, characterized by different glycemic indices and amylose-amylopectin content, on glucose metabolism in rat epididymal adipocytes. The two chosen starches were from mung bean (32% amylose) and cornstarch (0.5% amylose). The alpha-amylase digestibility was higher for the waxy cornstarch than that of the mung bean starch (60 +/- 4 vs. 45 +/- 3%, mean +/- SEM, respectively). The glycemic index of the waxy cornstarch diet (575 g starch /kg diet) was higher than that of the mung bean starch diet (107 +/- 7 vs. 67 +/- 5%, $P < 0.01$) when measured in vivo in two groups of normal rats ($n = 9$). In a subsequent study, normal and diabetic (streptozotocin-injected on d 2 of life) male Sprague-Dawley rats (18 per group) consumed a diet containing 575 g starch/kg diet as either waxy cornstarch or mung bean starch. After 3 wk, food intake, epididymal fat pad weights, and plasma glucose, insulin and triglyceride concentrations did not differ between diet groups. Adipocyte diameter was smaller in rats that consumed mung bean starch compared with those that consumed the waxy cornstarch diet ($P < 0.01$). The mung bean diet increased maximal insulin-stimulated ^{14}C -glucose oxidation (% of basal values, $P < 0.05$). In contrast, incorporation of ^{14}C -glucose into total lipids was significantly lower in rats that consumed the mung bean diet ($P < 0.05$).

We conclude that in both normal and diabetic rats, the chronic replacement of a high glycemic index starch by a low glycemic index one in a mixed diet increases insulin-stimulated glucose oxidation, decreases glucose incorporation into total lipids and decreases epididymal adipocyte diameter. Thus, the type of starch mixed into the diet has important metabolic consequences at the cellular level in both normal and diabetic rats.

PMID: 9430599 [PubMed - indexed for MEDLINE]

J Nutr. 2001 Jan;131(1):99-104. [Links](#)

High glycemic index starch promotes hypersecretion of insulin and higher body fat in rats without affecting insulin sensitivity.

[Pawlak DB](#),

[Bryson JM](#),

[Denver GS](#),

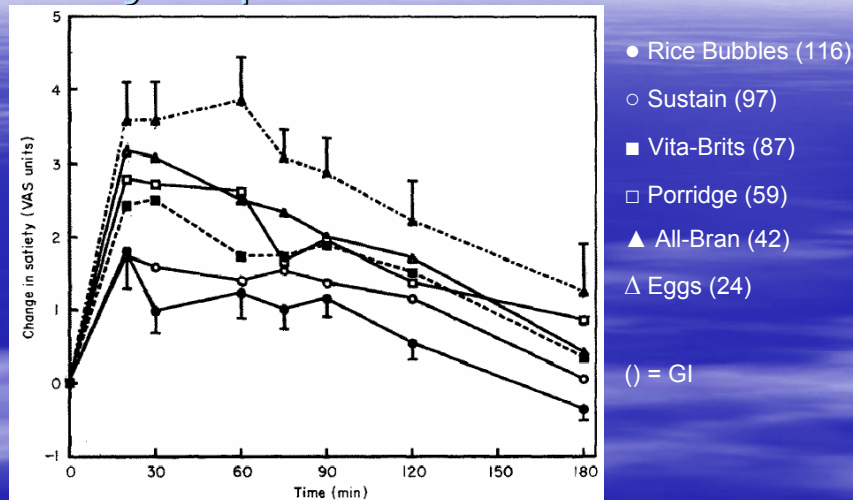
[Brand-Miller JC](#).

Human Nutrition Unit, Department of Biochemistry, The University of Sydney, NSW 2006, Australia.

In rats, prolonged feeding of high glycemic index (GI) starch results in basal hyperinsulinemia and an elevated insulin response to an intravenous glucose tolerance test (IVGTT). The aim of this study was to assess hepatic and peripheral insulin resistance (IR) using euglycemic hyperinsulinemic clamps. Insulin sensitivity, epididymal fat deposition and fasting leptin concentrations were compared in rats fed isocalorically a low or high GI diet for 7 wk (45% carbohydrate, 35% fat and 20% protein as energy) or a high fat diet (20% carbohydrate, 59% fat and 21% protein as energy) for 4 wk so that final body weights were similar. At the end of the study, high GI rats had higher basal leptin concentration and epididymal fat mass than the low GI group, despite comparable body weights. High GI and high fat feeding both resulted in the higher insulin response during IVGTT, but impaired glucose tolerance was seen only in rats fed high fat. The GI of the diet did not affect basal and clamp glucose uptake or hepatic glucose output, but high fat feeding induced both peripheral and hepatic IR. The findings suggest that hypersecretion of insulin without IR may be one mechanism for increased fat deposition in rats fed high GI diets.

PMID: 11208944 [PubMed - indexed for MEDLINE]

Satiety Response to various Test Meals



Holt S et al *Appetite*. 1992 Apr;18(2):129-41

Dr. C.P. Davis

Appetite. 1992 Apr;18(2):129-41. [Related Articles](#). [Links](#)

Relationship of satiety to postprandial glycaemic, insulin and cholecystokinin responses.

[Holt S](#), [Brand J](#), [Soveny C](#), [Hansky J](#).

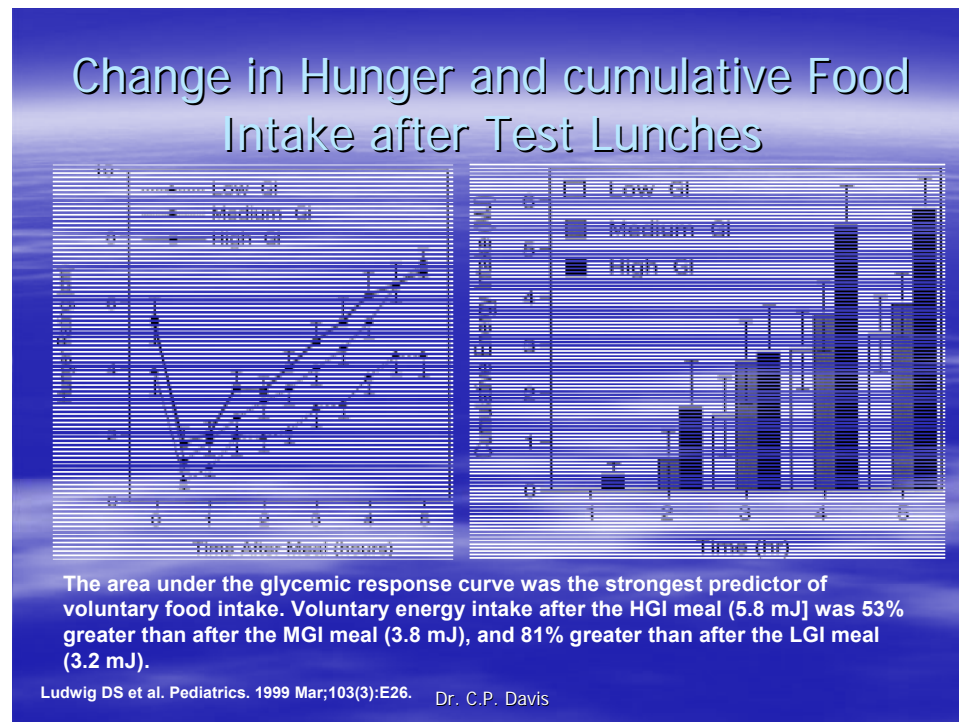
Department of Biochemistry, University of Sydney, Melbourne, Australia.

The effect of plasma glucose on satiety and the capacity of carbohydrates to stimulate cholecystokinin (CCK) remain unclear. The aim of this study was to test the hypothesis that the magnitude of the postprandial plasma glucose and insulin response is inversely related to the CCK response and to subjective satiety. Seven healthy, male volunteers consumed equal carbohydrate portions (0.5 g/kg body weight) of six test meals (Rice Bubbles, Sustain, Vita-Brits, All-Bran, porridge and white bread) in random order after an overnight fast. An egg and bacon meal was consumed as a non-carbohydrate control providing 0.5 g protein/kg body weight. Serum CCK, plasma glucose and insulin and subjective satiety (measured by a rating scale) were assessed over 3 h and quantified using the glycaemic index (GI), insulin index (II), the peak satiety score and area under the incremental curve (AUC). The observed GIs (mean \pm SE) ranged from 42.5 \pm 2.6 for All-Bran to 116.2 \pm 11.4 for Rice Bubbles, using white bread as the reference food (GI = 100). Peak satiety scores varied eightfold from 0.21 \pm 0.4 for Sustain to 1.64 \pm 0.4 for All-Bran. Significant inverse relationships were observed between the peak satiety score and both the glycaemic and insulin index of the seven meals ($r = -0.916$, p less than 0.001 and $r = -0.926$, p less than 0.001). A direct relationship was observed between satiety (AUC) and the CCK response (AUC) ($r = 0.73$, p less than 0.01). The results suggest that glycaemic and insulin responses to carbohydrate foods are inversely proportional to the CCK response and satiety.

Publication Types:

Clinical Trial

Randomized Controlled Trial



Pediatrics. 1999 Mar;103(3):E26. [Links](#)

High glycemic index foods, overeating, and obesity.

[Ludwig DS,](#)
[Majzoub JA,](#)
[Al-Zahrani A,](#)
[Dallal GE,](#)
[Blanco I,](#)
[Roberts SB.](#)

Division of Endocrinology, Department of Medicine, Children's Hospital, Boston, 300 Longwood Ave, Boston, MA 02115, USA.

OBJECTIVE: The prevalence of obesity has increased dramatically in recent years. However, the role of dietary composition in body weight regulation remains unclear. The purpose of this work was to investigate the acute effects of dietary glycemic index (GI) on energy metabolism and voluntary food intake in obese subjects. **METHODS:** Twelve obese teenage boys were evaluated on three separate occasions using a crossover study protocol. During each evaluation, subjects consumed identical test meals at breakfast and lunch that had a low, medium, or high GI. The high- and medium-GI meals were designed to have similar macronutrient composition, fiber content, and palatability, and all meals for each subject had equal energy content. After breakfast, plasma and serum concentrations of metabolic fuels and hormones were measured. Ad libitum food intake was determined in the 5-hour period after lunch. **RESULTS:** Voluntary energy intake after the high-GI meal (5.8 megajoule [mJ]) was 53% greater than after the medium-GI meal (3.8 mJ), and 81% greater than after the low-GI meal (3.2 mJ). In addition, compared with the low-GI meal, the high-GI meal resulted in higher serum insulin levels, lower plasma glucagon levels, lower postabsorptive plasma glucose and serum fatty acids levels, and elevation in plasma epinephrine. The area under the glycemic response curve for each test meal accounted for 53% of the variance in food intake within subjects. **CONCLUSIONS:** The rapid absorption of glucose after consumption of high-

GI meals induces a sequence of hormonal and metabolic changes that promote excessive food intake in obese subjects. Additional studies are needed to examine the relationship between dietary GI and long-term body weight regulation.

PMID: 10049982 [PubMed - indexed for MEDLINE]

Studies comparing glycemic response with changes in hunger, satiety or energy intake		
Reference	Modified dietary factor	Effect of low GI food
Haber et al. 1977 ¹	Apple, whole or processed	Increased satiety
Krotkiewski 1984	Guar gum	Decreased hunger
Spitzer and Rodin 1987	Fructose or glucose	Lower voluntary energy intake
Rodin et al. 1988	Fructose or glucose	Lower voluntary energy intake
Leathwood and Pollit 1988	Bean or potato	Decreased hunger
Rodin 1991	Fructose or glucose	Lower voluntary energy intake
Holt et al. 1992	Breakfast cereal	Increased satiety
van Amelsvoort and Weststrate 1992	Amylose or amylopectin	Increased satiety
Benini et al. 1995	Fiber added to meal	Decreased hunger
Gustafsson et al. 1995a	Vegetable type	Increased satiety
Gustafsson et al. 1995b	Raw or cooked carrots	Increased satiety
Holt and Miller 1995	Rice type	Lower voluntary energy intake
Lavin and Read 1995	Guar gum	Decreased hunger
Holt et al. 1996	38 individual foods	No change in satiety
Rigaud et al. 1998	Psyllium fiber	Lower voluntary energy intake
Ludwig et al. 1999a	Oatmeal type	Lower voluntary energy intake

Ludwig DS J Nutr. 2000 Feb;130(2S Suppl):280S-283S.
Dr. C.P. Davis

J Nutr. 2000 Feb;130(2S Suppl):280S-283S. Links

Dietary glycemic index and obesity.

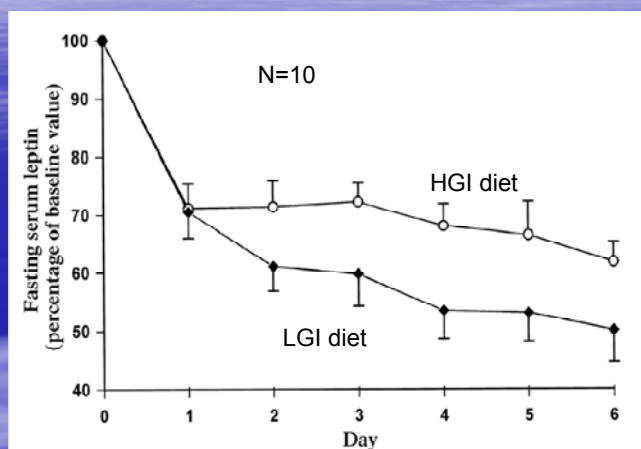
Ludwig DS.

Division of Endocrinology, Children's Hospital, Boston, MA 02115, USA.

Obesity is among the most important medical problems in America today. Currently, approximately 1 in 4 children and 1 in 2 adults are overweight, prevalence rates that have increased by 50% since the 1960s. In an attempt to combat this problem, the Federal government and various official medical agencies have advocated decreasing intake of total fat and sugar, while increasing consumption of "complex carbohydrate." Despite a recent reduction in fat consumption to near the recommended 30% of total energy, rates of obesity have continued to rise, suggesting that other dietary factors may play a critical role in body weight regulation. One such factor may be glycemic index. This review examines the physiologic effects of glycemic index and argues for the need for controlled clinical trials of a low glycemic index diet in the treatment of obesity.

PMID: 10721888 [PubMed - indexed for MEDLINE]

GI and Leptin



Mean (±SEM) daily fasting serum leptin as a percentage of baseline values.

Serum leptin decreased more rapidly and to a greater extent during the low-GI diet than during the high-GI diet ($P = 0.03$).

Note: Both diets had identical energy content.

Agus MS et al Am J Clin Nutr 2000;71:901-7

Dr. C.P. Davis

Am J Clin Nutr. 2000 Apr;71(4):901-7. [Links](#)

Dietary composition and physiologic adaptations to energy restriction.

[Agus MS](#),

[Swain JF](#),

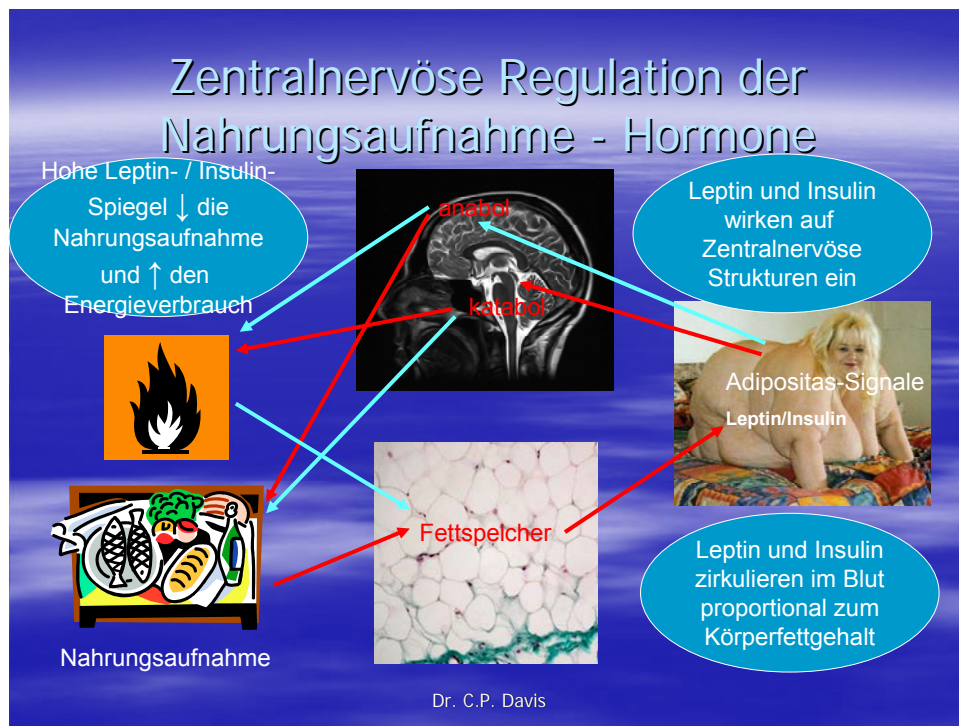
[Larson CL](#),

[Eckert EA](#),

[Ludwig DS](#).

Division of Endocrinology, Department of Medicine, Children's Hospital, Boston, and the General Clinical Research Center, Brigham and Women's Hospital, Boston, MA 02115, USA.

BACKGROUND: The concept of a body weight set point, determined predominantly by genetic mechanisms, has been proposed to explain the poor long-term results of conventional energy-restricted diets in the treatment of obesity. **OBJECTIVE:** The objective of this study was to examine whether dietary composition affects hormonal and metabolic adaptations to energy restriction. **DESIGN:** A randomized, crossover design was used to compare the effects of a high-glycemic-index (high-GI) and a low-glycemic-index (low-GI) energy-restricted diet. The macronutrient composition of the high-GI diet was (as percent of energy) 67% carbohydrate, 15% protein, and 18% fat and that of the low-GI diet was 43% carbohydrate, 27% protein, and 30% fat; the diets had similar total energy, energy density, and fiber contents. The subjects, 10 moderately overweight young men, were studied for 9 d on 2 separate occasions. On days -1 to 0, they consumed self-selected foods ad libitum. On days 1-6, they received an energy-restricted high- or low-GI diet. On days 7-8, the high- or low-GI diets were consumed ad libitum. **RESULTS:** Serum leptin decreased to a lesser extent from day 0 to day 6 with the high-GI diet than with the low-GI diet. Resting energy expenditure declined by 10.5% during the high-GI diet but by only 4.6% during the low-GI diet (7.38 ± 0.39 and 7.78 ± 0.36 MJ/d, respectively, on days 5-6; $P = 0.04$). Nitrogen balance tended to be more negative, and energy intake from snacks on days 7-8 was greater, with the high-GI than the low-GI diet. **CONCLUSION:** Diets with identical energy contents can have different effects on leptin concentrations, energy expenditure, voluntary food intake, and nitrogen balance, suggesting that the physiologic adaptations to energy restriction can be modified by dietary composition.



Moleküle regulieren das Gewicht 01.02.2002

Forschung, Klinik und Praxis 02/2002

Schlüsselwörter: Hypothalamus – Leptin – Neurotransmitter – Adipositas – Hunger- und Sättigungsregulation – Energiehomöostase

Die „Adipositasepidemie“

Jeder zweite Erwachsene in Deutschland ist übergewichtig, bis zu 20 % der Bevölkerung sind adipös. Dies wurde im WHOMONICA-Projekt ermittelt. Betroffen sind auch in gravierendem Maß Kinder und Jugendliche: Jedes 5. Kind und jeder 3. Jugendliche ist heute übergewichtig. Die Weltgesundheitsorganisation (WHO) spricht inzwischen sogar von einer „Adipositasepidemie“. Weltweit gilt Adipositas als das am schnellsten wachsende Gesundheitsrisiko. Wenn sich der derzeitige Trend weiterhin fortsetzt, dann wird im Jahr 2040 die Hälfte der erwachsenen Bevölkerung einen BMI über 30 kg/m² haben und damit übergewichtig sein. Die Folgen stehen drohend vor uns: Berechnungen ergeben beispielsweise für die Jahre 1995 bis 2025 einen Anstieg der Begleiterkrankung Diabetes mellitus Typ 2 um etwa 41 % (1).

Adipositas wird in hohem Maß vererbt, also nicht allein durch die Lebensbedingungen bestimmt. Zwillingsstudien an eineiigen Zwillingen, die getrennt voneinander in verschiedenen Familien aufgewachsen sind, zeigten dies deutlich: Etwa zwei Drittel der Zwillingspaare haben ein ähnliches Körpergewicht, obwohl sie in verschiedenen Familien aufgewachsen sind. Das bedeutet, dass bis zu 70 % der Adipositasentstehung genetisch mitbestimmt sein können. Weitere Studien zeigten, dass es tatsächlich physiologische Faktoren gibt, die das Risiko erhöhen, dick zu werden. Dazu gehört zum Beispiel ein niedriger Grundumsatz oder ein niedriges Niveau an Spontan-Aktivität (2, 3).

Beobachtungen aus vielen Familien, in denen sowohl schlanke als auch übergewichtige Kinder aufwachsen, werfen jedoch weitere Fragen auf. Wie kommt es, dass einige Menschen sowohl als Kind als auch als Erwachsener nach Lust und Laune essen können und ihr Gewicht

dennoch relativ konstant halten? Andere wiederum nehmen rapide zu, wenn sie ihrem natürlichen Hunger folgen. Kurz, wie reguliert der Körper Hunger, Appetit, Sättigung und auch das Gewicht?

Im Zentrum: der Hypothalamus

Energie- und Nahrungsaufnahme des Körpers werden ebenso wie der Energieumsatz im Gehirn gesteuert. Zur Gewichtsregulation muss das Gehirn zum einen den Energiezustand des Körpers incl. der gespeicherten Energie messen und andererseits Hunger und Sättigung regulieren und anpassen. Die dominierende Rolle bei diesem Prozess spielt der Hypothalamus. Er ist ein Teil des Zwischenhirns. Der Hypothalamus liegt unterhalb des Thalamus, einem lebenswichtigen Areal, das unter anderem die Körpertemperatur kontrolliert und den Wasserhaushalt reguliert.

Bereits vor 50 Jahren wurden im Hypothalamus zwei verschiedene Regionen mit entgegengesetzter Wirkung auf die Nahrungsaufnahme identifiziert: der ventromediale Hypothalamus (VMH), der als Sättigungszentrum fungiert, und der laterale Hypothalamus (LH) – das Hungerzentrum. Beide Regionen stehen in Kontakt miteinander. Ist das eine Zentrum aktiv, wird das andere gehemmt und umgekehrt (3).

Dennoch blieb lange Zeit unklar, wie die Hunger/Sättigungsregulation auf molekularer Ebene funktioniert. Mit der Klonierung des Leptingens im Jahr 1994 begann das Verständnis der molekularen Mechanismen dieser Regulation. Leptin meldet als peripheres Hormon des Fettgewebes den Zustand der Energiereserven des Körpers an das Zentralnervensystem (ZNS). Weitere Untersuchungen über die zentralen Wirkungen von Leptin führten schließlich zur Entdeckung von weiteren Stoffen und Arealen, die an der Energiebalance des Körpers beteiligt sind (2). Die Konsequenz aus diesen Entdeckungen: Die Regulation der Energiehomöostase ist wesentlich komplexer als bislang vermutet, und das einfache Bild vom Hunger- und Sättigungszentrum kann nicht mehr aufrecht erhalten werden (2, 3).

Regulation der Nahrungsaufnahme

Essen, also die Nahrungsaufnahme, ist der zentrale Teil der Energiehomöostase. Homöostase bedeutet in diesem Zusammenhang, dass der Körper versucht, langfristig seine Energiereserven und damit auch das Körpergewicht konstant zu halten. Er „verteidigt“ sein Gewicht („Set-Point-Theorie“). Dazu misst der Körper die Energiereserven und vergleicht sie mit der aktuellen Energieabgabe. Dieser Prozess stellt die *langfristige Nahrungsregulation* dar (4).

Die *kurzfristige Regulation* wird dagegen durch Hunger und Sättigung gesteuert. Hunger ist ein innerer Trieb, der zur Nahrungsaufnahme führt. Ist der Trieb befriedigt, treten Sättigung und Sätttheit ein. Als Sättigung wird das Ende der Nahrungsaufnahme bezeichnet. Sätttheit tritt erst nach Ende der Mahlzeit ein und beschreibt die Zeitdauer bis zum nächsten Hungergefühl. Über den Sättigungsmechanismus, der letztlich die Mahlzeitengröße bestimmt, ist bereits vieles bekannt. Weitgehend unbekannt ist bislang jedoch, wie die Intervalle zwischen den Mahlzeiten (Mahlzeitenfrequenz) reguliert werden.

Die Dehnung des Magens und des Darms sowie deren Inhalt sind die wichtigsten Sättigungssignale. Kaubewegungen sowie sensorische Informationen aus Nase, Mund, Rachen und Speiseröhre sind ebenfalls daran beteiligt (3, 6). Auf zwei Wegen erhält das Zentralnervensystem Informationen über die Nahrungszusammensetzung: über den Vagusnerv, der mit feinen Verästelungen den Verdauungskanal durchzieht sowie über endokrine (hormonproduzierende) Zellen des Darmepithels.

Beide Wege ermöglichen eine Chemorezeption. Bestimmte Fasern des Vagus werden z. B. nur durch kurzkettige Fettsäuren, andere durch kurzkettige Fettsäuren und Glycerin gereizt. Diese Reizung führt schließlich zu einem Nervenimpuls im ZNS. Die endokrinen Zellen werden ebenfalls durch einen ZNS-Impuls erreicht, allerdings auf indirektem Weg: Sie reagieren auf Magensäure, Aminosäuren oder Zucker mit der Freisetzung von Peptidhormonen, kleinen Proteinen mit Hormonwirkung, wie z. B. Cholezystokinin (CCK).

CCK reizt dann wiederum den Vagusnerv. Denkbar ist auch, dass CCK via Blut direkt in den Hypothalamus gelangt (3). Weitere Peptide, die am Sättigungssignal mitwirken, sind in Tabelle 1 genannt.

Über den kurzfristigen, gastrointestinalen Zustand hinausgehend informieren zwei weitere Sättigungsmechanismen den Körper über seine Energievorräte. Sie messen einerseits den Glykogenvorrat – den kurzfristigen Energiespeicher – und andererseits die Fettspeicher, das langfristige Energiedepot. Für diese Mechanismen wurden die „glukostatische“ und „lipostatische“ Theorie aufgestellt.

Die glukostatische Theorie

Für diesen Sättigungsmechanismus wird die Glukosekonzentration im Blut vom Hypothalamus registriert. Tatsächlich wurden inzwischen im Hypothalamus Neurone entdeckt, die die Glukosekonzentration messen können. Sie werden als Glukosensoren bezeichnet. Glukosensoren werden aber auch im Stammhirn und in der Leber gefunden. Die Glukosensoren der Leber können den Glukosegehalt des Blutes bestimmen, das direkt vom Darm in die Leber gelangt. Sie messen also die mit der Nahrungsaufnahme im Zusammenhang stehenden Schwankungen in der Glukosekonzentration. Tatsächlich führt im Versuch eine Infusion von Glukose an die Pfortader zur Unterdrückung der Nahrungsaufnahme. Die Informationen der Glukosensoren der Leber werden über den Vagusnerv ans ZNS gesendet. Hohe Glukosekonzentrationen tragen zur Sättigung, niedrige zum Entstehen von Hunger bei.

Die lipostatische Theorie

Nach dieser Theorie wird dem Gehirn mitgeteilt, wie gut der langfristige Energiezustand des Körpers in Form der Fettspeicher aussieht. Ein bahnbrechender Beweis für diese Theorie war die Entdeckung eines Proteins: Leptin. Es wird vom Fettgewebe produziert und ins Blut abgegeben. Je mehr Fettgewebe vorhanden ist, desto mehr Leptin wird produziert und desto höher ist die Blutkonzentration. Obwohl eine ganze Reihe von Sättigungssignalen bekannt sind, ist Leptin derzeit das einzig bekannte Langzeitsignal. In der Literatur wird es auch als Adipositas-Signal bezeichnet. Insulin könnte jedoch ebenfalls ein solches Signal sein, weil die Insulin-Blutkonzentration langfristig mit dem Fettgehalt korreliert. Außerdem bindet Insulin im ZNS an Neurone, die an der Energiehomöostase beteiligt sind (3).

Das neue Bild von Leptin

Die Entdeckung von Leptin löste zunächst Euphorie aus. Verlockend stand vor Augen, dass möglicherweise eine Leptininjektion Adipöse zur Gewichtsabnahme bringen könnte. Doch inzwischen haben sich solche Versuche als wenig effektiv erwiesen. Die Gewichtsabnahmen waren minimal.

Adipositas wird nicht durch einen Mangel an Leptin verursacht. Es ist vielmehr so, dass bei erhöhter Fettgewebsmasse (Adipositas) auch der Leptinspiegel im Blut erhöht ist. Das heißt, dass der Körper die Information über den Füllungszustand der Fettspeicher an das ZNS schickt. Das ZNS ist bei Adipösen jedoch nicht in der Lage, das Signal richtig, also mit einer reduzierten Nahrungsaufnahme, zu beantworten. Hierfür wurde inzwischen der Begriff Insulinresistenz eingeführt (4). Wie und warum es zu dieser Resistenz kommt, ist noch unverstanden und wird derzeit intensiv erforscht.

Nach heutigem Kenntnisstand hat Leptin nicht – wie ursprünglich vermutet – die Aufgabe, den Körper vor zuviel Nahrungsaufnahme zu schützen, sondern im Gegenteil Nahrungsmangel zu verhindern. Tritt ein Leptinmangel auf, dann reagiert der Körper mit Hungergefühlen, während ein Überschuss nicht zwangsläufig den Appetit reduziert.

Außerdem hat Leptin eine Bedeutung für das Immunsystem und die Fruchtbarkeit. Beide Körperfunktionen sind sehr energieaufwändig. Sind die Fettspeicher leer und somit kein oder nur wenig Leptin im Blut, dann werden diese beiden Körperfunktionen gedrosselt, um Energie zu sparen und das Überleben zu sichern (3). Typisches Beispiel für diesen Prozess ist die Anorexie. Bei anorektischen Frauen bleibt die Regelblutung aus. Auch bei pubertären

Mädchen beginnt die Regelblutung erst, wenn der Körper einen bestimmten kritischen Fettgehalt überschritten hat. So stellt die Natur sicher, dass eine Schwangerschaft erst eintritt, wenn die Mutter genügend Energiereserven aufgebaut hat (7).

Trotz dieser wichtigen Aufgaben scheint Leptin nicht essentiell zu sein. Zum Beispiel werden Mäuse mit einem Leptindefekt zwar extrem adipös und steril, können aber dennoch überleben. Auch die wenigen bekannten Menschen mit Leptinmangel sind extrem fettleibig und wahrscheinlich nicht fortpflanzungsfähig, zeigen ansonsten jedoch wenig andere pathologische Erscheinungen (3).

Informationszentrale Hypothalamus

Bereits kurz nach der Entdeckung von Leptin wurde auch der Rezeptor gefunden, der das Leptinsignal an die Zellen weitergibt. Der OB-Rb genannte Rezeptor existiert sowohl im Hypothalamus als auch in vielen anderen Zellen wie Muskelzellen, Leberzellen, Pankreaszellen u.s.w. Die Wirkung auf das Appetitsystem wird aber ausschließlich durch die Bindung von Leptin an die Rezeptoren im Hypothalamus vermittelt. Hier stimuliert oder inhibiert Leptin die Ausschüttung verschiedener Neuropeptide (5).

Der Hypothalamus verarbeitet aber nicht nur diese eine Information. Er fungiert vielmehr als Schaltzentrale für alle körpereigenen (internen) und äußeren (externe) Reize, wie Geruch, Geschmack etc. Alle Signale, die über den Körperzustand berichten, also sowohl aus Drüsen (humorale) als auch aus dem peripheren Nervensystem (nervöse) freigesetzte, werden im Hypothalamus mit den Signalen verrechnet, die über die externen Bedingungen informieren. Dieser Prozess wird als Integration bezeichnet.

Hypothalamische Kerne und Zonen

Der Hypothalamus besitzt eine Reihe von lokalen Ansammlungen von Neuronen, so genannte Kerne, und weniger gut voneinander abgegrenzte Gebiete, die auf Grund ihrer Lage in drei funktionelle Gruppen eingeteilt werden können: in die periventrikuläre, mediale und laterale Zone.

Die einfache Vorstellung eines ventromedialen Sättigungs- (VMH) und eines lateralen Hungerzentrums (LH) ist angesichts moderner Erkenntnisse nicht mehr haltbar:

Beispielsweise resultiert aus einer Verletzung im LH nicht nur eine Störung der Nahrungsaufnahme, sondern auch ein vollständiges Ignorieren aller Außenreize, also ein kompletter Motivationsverlust. Darüber hinaus führten Schädigungen am VMH nicht zum Überessen, wenn gleichzeitig der Vagusnerv durchtrennt wurde. Außerdem kann mittlerweile ausgeschlossen werden, dass sich das Hunger- und das Sättigungszentrum gegenseitig hemmen. Vielmehr wurde entdeckt, dass beide Zentren mit dem dorsomedialen hypothalamischen Nukleus (DMH), dem Nukleus Arcuatus (ARC) und dem Nukleus Paraventricularis (PVN) verbunden sind. Die Nahrungsaufnahme wird also nicht von zwei Zentren allein gesteuert, sondern durch ein komplexes Netzwerk (orexisches Netzwerk). Dieses Netzwerk dient als Integrationszentrum zur Kontrolle der Nahrungsaufnahme und der Energiehomöostase. Ihm gehören mindestens der PVN, DMH, VMH, LH und ARC an (5).

Signalüberträger im Hypothalamus

Signale zwischen Nervenzellen werden über Neurotransmitter und Neuropeptide übertragen. Das ZNS benutzt jedoch für viele seiner Funktionen die gleichen Transmitter. Keiner ist allein für eine spezielle Aufgabe zuständig. Sie verwenden auch in der Regel nicht nur eine Art Bindungsmolekül, also Rezeptoren. Für die spezifische Wirkung kommt es auf die genaue Kombination von Transmitter und Rezeptor an. Welche Transmitter könnten also in der Regulation der Nahrungsaufnahme eine Rolle spielen? Tabelle 1 nennt die wichtigsten bekannten Neurotransmitter und Neuropeptide und ihre wahrscheinliche Funktion in Bezug auf die Nahrungsaufnahme.

Noradrenalin kann als einziger Transmitter sowohl die Nahrungsaufnahme anregen als auch unterbinden, je nachdem auf welche Rezeptoren er trifft. Im PVN stimuliert er nicht nur die Nahrungsaufnahme, sondern steigert selektiv die Aufnahme von Kohlenhydraten. Das Peptid

Galanin verstärkt die Fettaufnahme und Opiod-Peptide erhöhen die Proteinaufnahme. Neuropeptid Y (NPY) ist derzeit der stärkste bekannte Stimulator des „Fressverhaltens“. Wird NPY in das PVN injiziert, dann wird sogar bei gesättigten Tieren die Aufnahme von Nahrung – insbesondere Kohlenhydraten – erreicht. Parallel dazu wird die energieverbrauchende Wärmeerzeugung gedrosselt. Bei Nahrungsentzug wird verstärkt NPY freigesetzt, Nahrungsaufnahme reduziert NPY.

Das Corticotropin-freisetzende Hormon (CRH) ist der Gegenspieler von NPY. Es wirkt katabol, weil es im PVN die Nahrungsaufnahme bremst und den Energieverbrauch erhöht. Gleichzeitig bewirkt es die Stressantwort durch Freisetzen von Stresshormonen aus der Hypophyse. Leptin stimuliert wiederum die Biosynthese und Freisetzung von CRH (5).

Tab. 1: Neuropeptide, die die Nahrungsaufnahme beeinflussen (3).stimulierend (orexigen):

Neuropeptide Y (NPY)

Melanin concentrating hormone (MCH)

Agouti related peptide (AGRP)

Galanin

Orexin A und B

β -Endorphin

Opiode

Noradrenalin (α 2-Rezeptor)

Gamma-Amino-Buttersäure (GABA)

Ghrelinvermindernd (anorexigen):

Melanocyte stimulation hormone (α -MSH)

Corticotropin releasing factor (CRF)

Cocaine and amphetamine-regulated transcript (CART)

Glucagon like peptide 1 (GLP-1)

Glukagon

Thyrotropin releasing hormone (TRH)

Interleukin β (IL- β)

Cholecystokinin (CCK)

Urocortin

Neurotensin

Enterostatin

Amylin

Oxytocin

Bombensin

SerotoninDopamin

Histamin

Noradrenalin (α 1-Rezeptor, β 1-Rezeptor)

Der POMC/MC-Signalweg

Neben dem Leptin-Rezeptor kommt vor allem dem α ,-Melanozyten-stimulierenden-Hormon (α -MSH) eine bedeutende regulierende Rolle zu. Es gehört zu einem weiteren Signalweg – dem hypothalamischen Melanocortin(MC)-Weg. Die Peptide dieses Weges gehen aus einem Vorläufer-Polypeptid (Proiomelanocortin = POMC), der im ARC des Hypothalamus synthetisiert wird, hervor. Die Peptide haben völlig unterschiedliche Wirkungen. α -MSH ist eines davon. Außer der Aktivierung der Melanozyten, die an der Haarfarbenbildung beteiligt sind, besitzt es eine Funktion bei der Appetitregulation. α -MSH bindet aber auch an den so genannten MC4-Rezeptor, der wiederum den Stoffwechsel beschleunigt und eine gesteigerte Fettverbrennung sowie eine Reduktion des Appetits bewirkt. Dieser Zusammenhang mit der Gewichtsregulation des Menschen konnte kürzlich bei extrem adipösen Patienten bestätigt

werden. Patienten mit einer Mutation im POMC-Gen oder MC4-Rezeptor-Gen zeigen eine schwere und früh beginnende, extreme Adipositas (2, 8).

Bislang unbekannte Neuropeptide

Zusätzlich zu den bereits erwähnten Neuropeptiden mit Wirkung auf die Regulation der Energiebilanz und Appetit im Hypothalamus wurden kürzlich einige andere Peptide mit ähnlichen Wirkungen beschrieben. Dazu zählen das Melanin-konzentrierende Hormon (MCH), Glucagon-like-peptide 1 (GLP1), Galanin oder Neurotensin.

Ein sehr interessantes, neu entdecktes Neuropeptid ist das Cocain- und Amphetamin-regulierte Transkript, kurz CART. Dieses Peptid bewirkt eine starke Hemmung der Nahrungsaufnahme und hemmt die NPY-induzierte Nahrungszufuhr vollständig. CART ist mit POMC in Neuronen des ARC und benachbarten Regionen verschaltet. Die CART/POMC-Nervenzellen sind Leptin-sensitiv. Die bisher vorliegenden Befunde deuten darauf hin, dass die Verschaltung zum Leptin-System zur Steigerung von Thermogenese, Energieverbrauch und reduziertem Körpergewicht beiträgt.

Energiehomöostase kompliziert reguliert

Das Bild, das sich derzeit von der Regulation der Energiehomöostase und des Körpergewichtes sowie von Hunger und Sättigung abzeichnet, ist extrem komplex. Noch sind nicht alle Teilnehmer auf molekularer Ebene identifiziert. Als gesichert kann angesehen werden, dass die Nahrungsaufnahme über etliche Kurzzeit- und Langzeitsignale aus dem Körper und der Umwelt gesteuert wird, und dass der Hypothalamus, der als „Zentralcomputer“ angesehen werden kann, das Zentrum der Steuerung ist. Leptin als Indikator des Fettspeichers, aber auch Glukose, aktivierten bestimmte Nervenzellen in hypothalamischen Kernen und Gebieten. Unter diesen haben sich ARC, VMH und DMH als essentiell erwiesen. Diese Aktivierung setzt die teilweise beschriebenen Signalwege in Gang. Die Beteiligung von derart vielen und verschiedenen Peptiden, Transmittern etc. an der Regulation von Gewicht, Energiehomöostase, Hunger und Sättigung zeigen, dass die Entstehung einer Adipositas möglicherweise durch viele Gene bestimmt wird. Bisherige Genomkartierungen deuten auf eine Vielzahl von Orten auf verschiedenen Chromosomen hin, die vielleicht eine Rolle spielen. Möglicherweise wirkt sich eine komplizierte Regulation und körperliche Ausstattung, die in Notzeiten das Überleben sichert, im Überfluss nachteilig aus. Derzeit ist die Suche nach einer medikamentösen Therapie der Adipositas im Gange. Sie konzentriert sich auf Medikamente, die über eine Beeinflussung der Neurotransmitter den Hunger unterdrücken. Angesichts der zahlreichen Wirkungen untereinander und der komplizierten Regulation scheint das Ergebnis dieser Suche jedoch nicht unproblematisch. Unerwünschte Wirkungen sind denkbar (4, 5).

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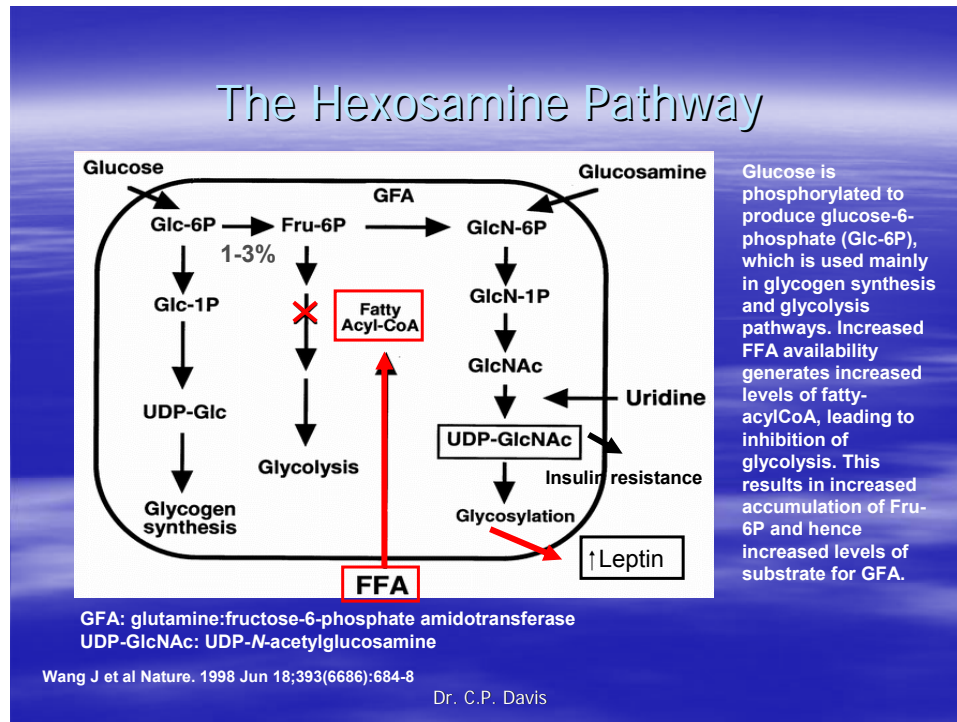
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A nutrient-sensing pathway regulates leptin gene expression in muscle and fat.

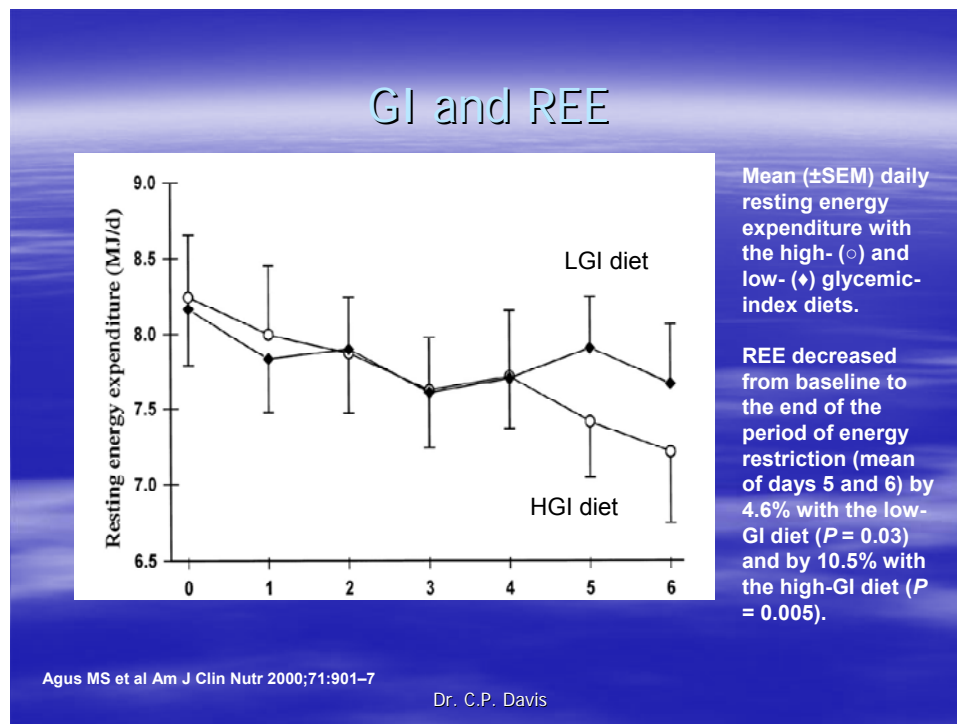
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Leptin, the protein encoded by the obese (ob) gene, is synthesized and released in response to increased energy storage in adipose tissue. However, it is still not known how incoming energy is sensed and transduced into increased expression of the ob gene. The hexosamine biosynthetic pathway is a cellular 'sensor' of energy availability and mediates the effects of glucose on the expression of several gene products. Here we provide evidence for rapid activation of ob gene expression in skeletal muscle by glucosamine. Increased tissue concentrations of the end product of the hexosamine biosynthetic pathway, UDP-N-acetylglucosamine (UDP-GlcNAc), result in rapid and marked increases in leptin messenger RNA and protein levels (although these levels were much lower than those in fat). Plasma leptin levels and leptin mRNA and protein levels in adipose tissue also increase. Most important, stimulation of leptin synthesis is reproduced by either hyperglycaemia or hyperlipidaemia, which also increase tissue levels of UDP-N-acetylglucosamine in conscious rodents. Finally, incubation of 3T3-L1 pre-adipocytes and L6 myocytes with glucosamine rapidly induces ob gene expression. Our findings are the first evidence of inducible leptin

expression in skeletal muscle and unveil an important biochemical link between increased availability of nutrients and leptin expression.

PMID: 9641678 [PubMed - indexed for MEDLINE]



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Dietary composition and physiologic adaptations to energy restriction.

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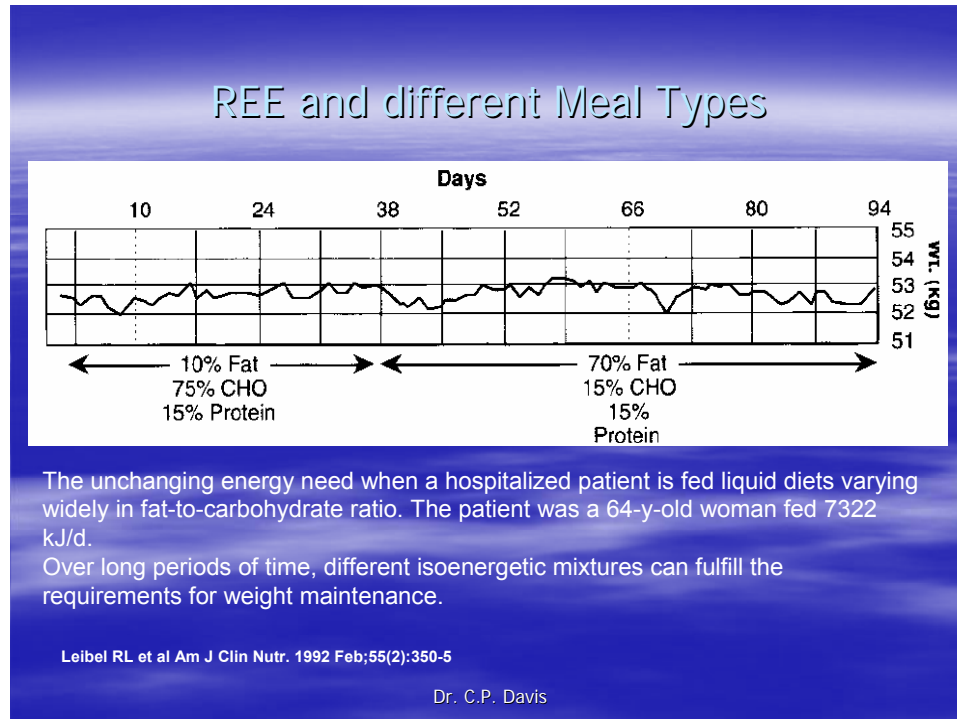
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BACKGROUND: The concept of a body weight set point, determined predominantly by genetic mechanisms, has been proposed to explain the poor long-term results of conventional energy-restricted diets in the treatment of obesity. **OBJECTIVE:** The objective of this study was to examine whether dietary composition affects hormonal and metabolic adaptations to energy restriction. **DESIGN:** A randomized, crossover design was used to compare the effects of a high-glycemic-index (high-GI) and a low-glycemic-index (low-GI) energy-restricted diet. The macronutrient composition of the high-GI diet was (as percent of energy) 67% carbohydrate, 15% protein, and 18% fat and that of the low-GI diet was 43% carbohydrate, 27% protein, and 30% fat; the diets had similar total energy, energy density, and fiber contents. The subjects, 10 moderately overweight young men, were studied for 9 d on 2 separate occasions. On days -1 to 0, they consumed self-selected foods ad libitum. On days 1-6, they received an energy-restricted high- or low-GI diet. On days 7-8, the high- or low-GI diets were consumed ad libitum. **RESULTS:** Serum leptin decreased to a lesser extent from day 0 to day 6 with the high-GI diet than with the low-GI diet. Resting energy expenditure declined by 10.5% during the high-GI diet but by only 4.6% during the low-GI diet (7.38 ± 0.39 and 7.78 ± 0.36 MJ/d, respectively, on days 5-6; $P = 0.04$). Nitrogen balance tended to be more negative, and energy intake from snacks on days 7-8 was greater, with the high-GI

than the low-GI diet. **CONCLUSION:** Diets with identical energy contents can have different effects on leptin concentrations, energy expenditure, voluntary food intake, and nitrogen balance, suggesting that the physiologic adaptations to energy restriction can be modified by dietary composition.

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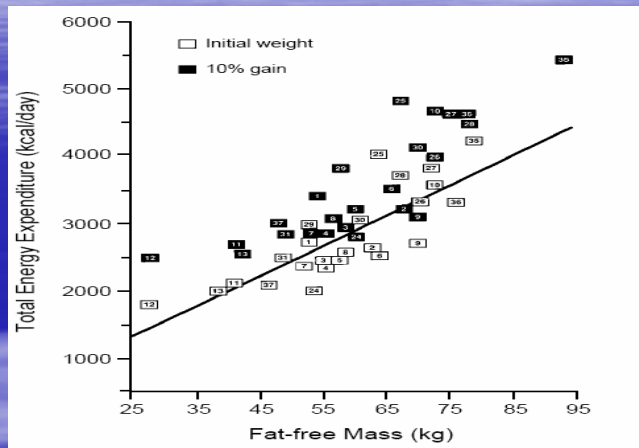
[Checani GC](#).

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Diets rich in fat may promote obesity by leading to a greater deposition of adipose-tissue triglycerides than do isoenergetic diets with less fat. This possibility was examined by a retrospective analysis of the energy needs of 16 human subjects (13 adults, 3 children) fed liquid diets of precisely known composition with widely varied fat content, for 15-56 d (33 \pm 2 d, mean \pm SE). Subjects lived in a metabolic ward and received fluid formulas with different fat and carbohydrate content, physical activity was kept constant, and precise data were available on energy intake and daily body weight. Isoenergetic formulas contained various percentages of carbohydrate as cerelese (low, 15%; intermediate, 40% or 45%; high, 75%, 80%, or 85%), a constant 15% of energy as protein (as milk protein), and the balance of energy as fat (as corn oil). Even with extreme changes in the fat-carbohydrate ratio (fat energy varied from 0% to 70% of total intake), there was no detectable evidence of significant variation in energy need as a function of percentage fat intake.

PMID: 1734671 [PubMed - indexed for MEDLINE]

TEE and BW



The relation of total energy expenditure (TEE), as measured by the amount of energy required to keep weight constant, with fat-free mass (FFM).

A 10 percent increase in the usual weight was accompanied by a 16 percent increase in 24-hour total energy expenditure.

Leibel RL et al N Engl J Med. 1995 Mar 9;332(10):621-8

Dr. C.P. Davis

N Engl J Med. 1995 Mar 9;332(10):621-8. [Links](#)

Erratum in:

N Engl J Med 1995 Aug 10;333(6):399.

Comment in:

[N Engl J Med. 1995 Mar 9;332\(10\):673-4.](#)

Changes in energy expenditure resulting from altered body weight.

[Leibel RL](#),

[Rosenbaum M](#),

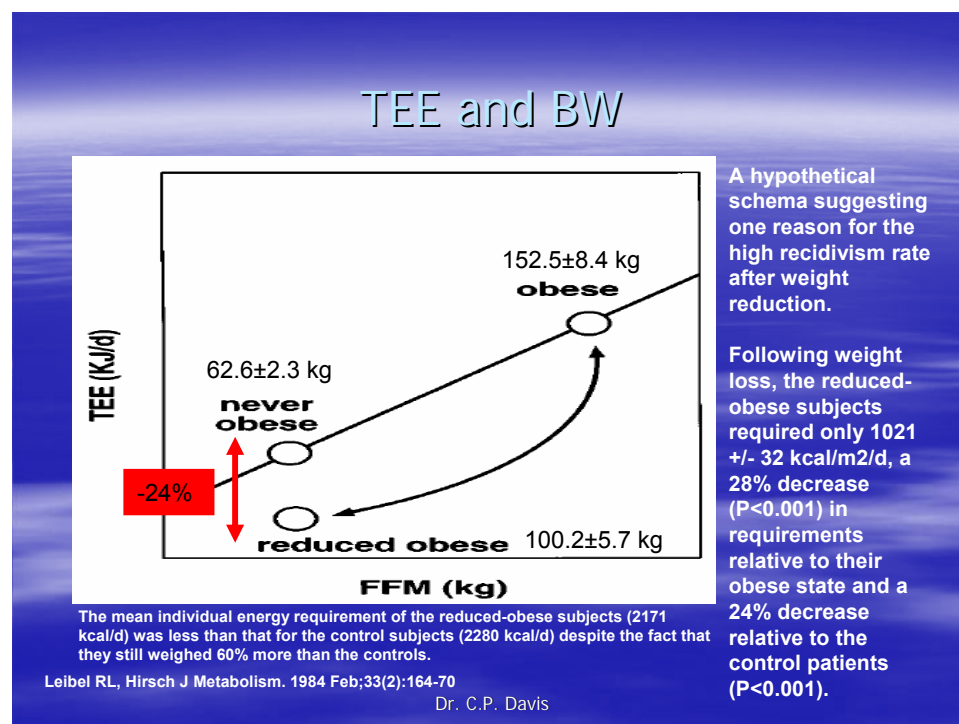
[Hirsch J](#).

Laboratory of Human Behavior and Metabolism, Rockefeller University, New York, NY 10021.

BACKGROUND. No current treatment for obesity reliably sustains weight loss, perhaps because compensatory metabolic processes resist the maintenance of the altered body weight. We examined the effects of experimental perturbations of body weight on energy expenditure to determine whether they lead to metabolic changes and whether obese subjects and those who have never been obese respond similarly. **METHODS.** We repeatedly measured 24-hour total energy expenditure, resting and nonresting energy expenditure, and the thermic effect of feeding in 18 obese subjects and 23 subjects who had never been obese. The subjects were studied at their usual body weight and after losing 10 to 20 percent of their body weight by underfeeding or gaining 10 percent by overfeeding. **RESULTS.** Maintenance of a body weight at a level 10 percent or more below the initial weight was associated with a mean (\pm SD) reduction in total energy expenditure of 6 ± 3 kcal per kilogram of fat-free mass per day in the subjects who had never been obese ($P < 0.001$) and 8 ± 5 kcal per kilogram per day in the obese subjects ($P < 0.001$). Resting energy expenditure and nonresting energy expenditure each decreased 3 to 4 kcal per kilogram of fat-free mass per day in both groups of subjects. Maintenance of body weight at a level 10 percent above the usual weight was associated with an increase in total energy expenditure of 9 ± 7 kcal per kilogram of fat-free mass per day in the subjects who had never been obese ($P < 0.001$) and 8 ± 4 kcal per kilogram per day in the obese subjects ($P < 0.001$). The thermic effect of feeding and nonresting energy expenditure increased by approximately 1 to 2 and 8 to 9 kcal per kilogram of fat-free mass

per day, respectively, after weight gain. These changes in energy expenditure were not related to the degree of adiposity or the sex of the subjects. **CONCLUSIONS.** Maintenance of a reduced or elevated body weight is associated with compensatory changes in energy expenditure, which oppose the maintenance of a body weight that is different from the usual weight. These compensatory changes may account for the poor long-term efficacy of treatments for obesity.

PMID: 7632212 [PubMed - indexed for MEDLINE]



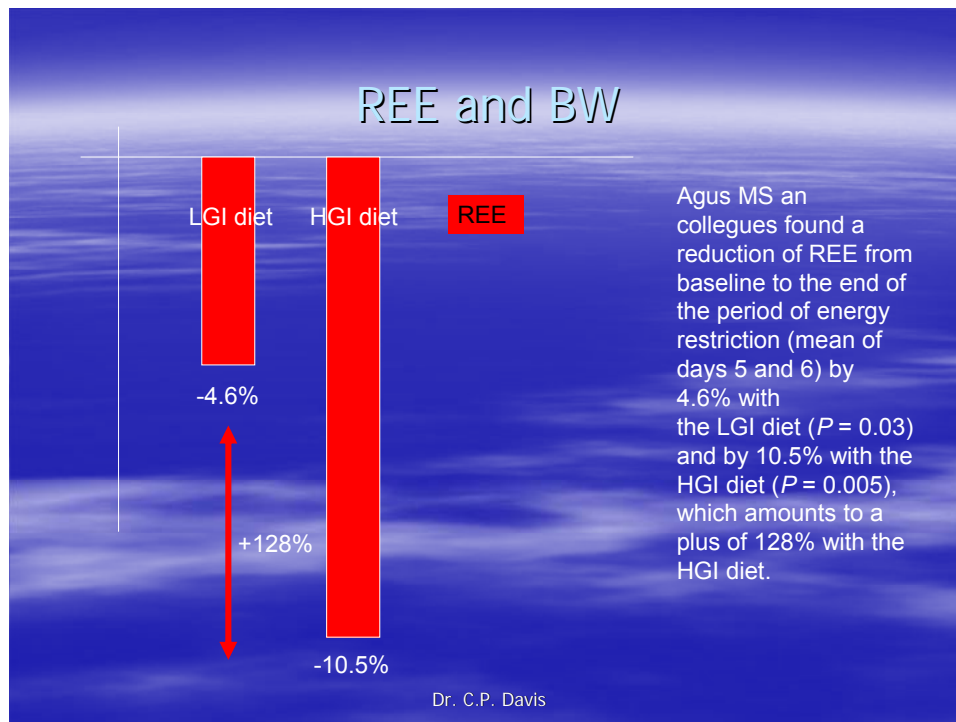
Metabolism. 1984 Feb;33(2):164-70. [Links](#)

Diminished energy requirements in reduced-obese patients.

[Leibel RL](#),
[Hirsch J](#).

In assessing the reasons for the frequent regaining of weight by reduced-obese patients, we examined retrospectively the seven-day energy intake requirements for weight maintenance of 26 obese patients (12 males, 14 females) at maximum weight (152.5 \pm 8.4 kg) and after weight loss (100.2 \pm 5.7 kg). These results were compared with those obtained in 26 age- and sex-matched control patients who had never been obese (62.6 \pm 2.3 kg). The obese and control subjects required comparable caloric intakes: 1432 \pm 32 kcal/m²/d vs 1341 \pm 33 kcal/m²/d, respectively. Following weight loss, the reduced-obese subjects required only 1021 \pm 32 kcal/m²/d, a 28% decrease (P less than 0.001) in requirements relative to their obese state and a 24% decrease relative to the control patients (P less than 0.001). The mean individual energy requirement of the reduced-obese subjects (2171 kcal/d) was less than that for the control subjects (2280 kcal/d) despite the fact that they still weighed 60% more than the controls. In order to maintain a reduced weight, some reduced-obese or even partially reduced patients must restrict their food intake to approximately 25% less than that anticipated on the basis of metabolic body size. The reasons why this finding is unlikely to be an artifactual consequence of changes in lean body mass or body water content are discussed. This finding has implications with regard to the pathophysiology and treatment of obesity in humans.

PMID: 6694559 [PubMed - indexed for MEDLINE]



Am J Clin Nutr. 2000 Apr;71(4):901-7. [Links](#)

Dietary composition and physiologic adaptations to energy restriction.

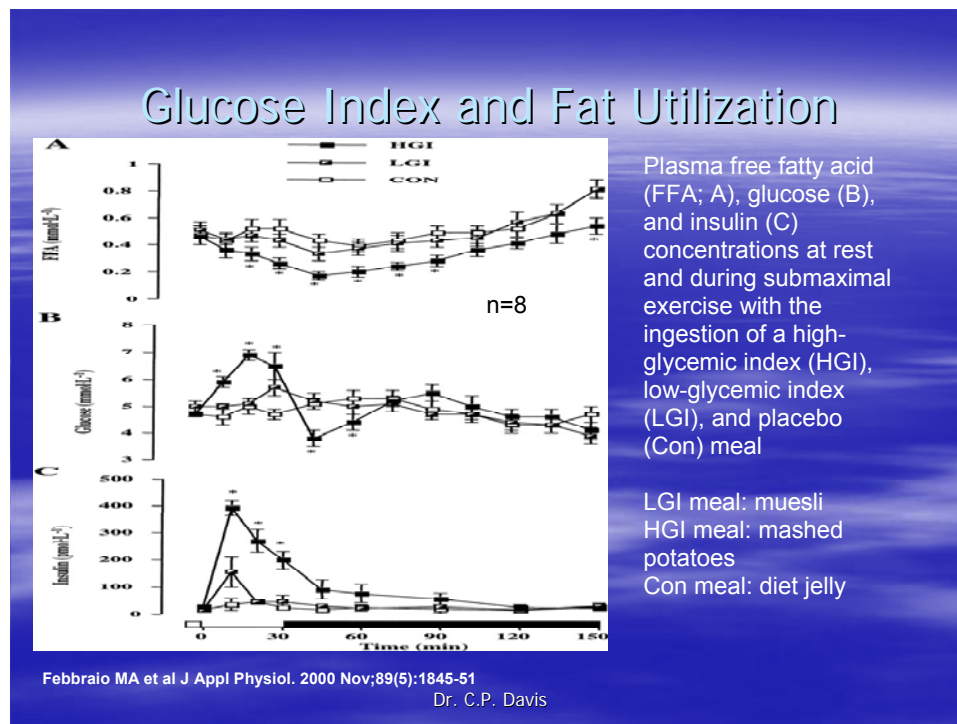
**Agus MS,
Swain JF,
Larson CL,
Eckert EA,
Ludwig DS.**

Division of Endocrinology, Department of Medicine, Children's Hospital, Boston, and the General Clinical Research Center, Brigham and Women's Hospital, Boston, MA 02115, USA.

BACKGROUND: The concept of a body weight set point, determined predominantly by genetic mechanisms, has been proposed to explain the poor long-term results of conventional energy-restricted diets in the treatment of obesity. **OBJECTIVE:** The objective of this study was to examine whether dietary composition affects hormonal and metabolic adaptations to energy restriction. **DESIGN:** A randomized, crossover design was used to compare the effects of a high-glycemic-index (high-GI) and a low-glycemic-index (low-GI) energy-restricted diet. The macronutrient composition of the high-GI diet was (as percent of energy) 67% carbohydrate, 15% protein, and 18% fat and that of the low-GI diet was 43% carbohydrate, 27% protein, and 30% fat; the diets had similar total energy, energy density, and fiber contents. The subjects, 10 moderately overweight young men, were studied for 9 d on 2 separate occasions. On days -1 to 0, they consumed self-selected foods ad libitum. On days 1-6, they received an energy-restricted high- or low-GI diet. On days 7-8, the high- or low-GI diets were consumed ad libitum. **RESULTS:** Serum leptin decreased to a lesser extent from day 0 to day 6 with the high-GI diet than with the low-GI diet. Resting energy expenditure declined by 10.5% during the high-GI diet but by only 4.6% during the low-GI diet (7.38 ± 0.39 and 7.78 ± 0.36 MJ/d, respectively, on days 5-6; $P = 0.04$). Nitrogen balance tended to be more negative, and energy intake from snacks on days 7-8 was greater, with the high-GI than the low-GI diet. **CONCLUSION:** Diets with identical energy contents can have different effects on leptin concentrations, energy expenditure, voluntary food intake, and nitrogen

balance, suggesting that the physiologic adaptations to energy restriction can be modified by dietary composition.

PMID: 10731495 [PubMed - indexed for MEDLINE]



J Appl Physiol. 2000 Nov;89(5):1845-51. Links

Preexercise carbohydrate ingestion, glucose kinetics, and muscle glycogen use: effect of the glycemic index.

[Febbraio MA](#),

[Keenan J](#),

[Angus DJ](#),

[Campbell SE](#),

[Garnham AP](#).

Exercise Physiology and Metabolism Laboratory, Department of Physiology, The University of Melbourne, Parkville 3052, Australia. m.febbraio@physiology.unimelb.edu.au

Eight trained men cycled at 70% peak oxygen uptake for 120 min followed by a 30-min performance cycle after ingesting either a high-glycemic index (HGI), low-glycemic index (LGI), or placebo (Con) meal 30 min before exercise. Ingestion of HGI resulted in an elevated ($P < 0.01$) blood glucose concentration compared with LGI and Con. At the onset of exercise, blood glucose fell ($P < 0.05$) such that it was lower ($P < 0.05$) in HGI compared with LGI and Con at 15 and 30 min during exercise. Plasma insulin concentration was higher ($P < 0.01$) throughout the rest period after ingestion of HGI compared with LGI and Con. Plasma free fatty acid concentrations were lower ($P < 0.05$) throughout exercise in HGI compared with LGI and Con. The rates of [6,6-(2)H]glucose appearance and disappearance were higher ($P < 0.05$) at rest after ingestion and throughout exercise in HGI compared with LGI and Con.

Carbohydrate oxidation was higher ($P < 0.05$) throughout exercise, whereas glycogen use tended ($P = 0.07$) to be higher in HGI compared with LGI and Con. No differences were observed in work output during the performance cycle when comparing the three trials. These results demonstrate that preexercise carbohydrate feeding with a HGI, but not a LGI, meal augments carbohydrate utilization during exercise but does not effect exercise performance.

PMID: 11053335 [PubMed - indexed for MEDLINE]

Ways through which LGI Foods may promote Weight Control

- Promoting satiety
 - Longer transit time results in prolonged feedback time of anorexigenic hormones to the satiety center in the brain
- Promoting fat oxidation at the expense of CHO oxidation
 - Acute increase in glucose and insulin leads to activation of CHO oxidation through the rapid activation of key-rate limiting enzymes
 - e.g. malonyl-CoA, an intermediate of glucose oxidation, strongly inhibits fatty acid transport into mitochondria, resulting in decreased fatty acid oxidation
 - Chronic hyperglycemia and hyperinsulinemia alters the expression of key-rate limiting enzymes (e.g. carnitine palmitoyl transferase) and, thus, fat oxidation
 - Simoneau JA et al: in obesity-related insulin resistance, the metabolic capacity of skeletal muscle appears to be organized toward fat esterification rather than oxidation and dietary-induced weight loss does not correct this disposition

Brand-Miller JC et al Am J Clin Nutr. 2002 Jul;76(1):281S-5S

Simoneau JA et al FASEB J. 1999 Nov;13(14):2051-60

Weyer C et al J Clin Endocrinol Metab. 2000 Mar;85(3):1087-94

Dr. C.P. Davis

Am J Clin Nutr. 2002 Jul;76(1):281S-5S. Links

Glycemic index and obesity.

Brand-Miller JC,

Holt SH,

Pawlak DB,

McMillan J.

Human Nutrition Unit, School of Molecular and Microbial Biosciences, University of Sydney, NSW, Australia. j.brandmiller@biochem.usyd.edu.au

Although weight loss can be achieved by any means of energy restriction, current dietary guidelines have not prevented weight regain or population-level increases in obesity and overweight. Many high-carbohydrate, low-fat diets may be counterproductive to weight control because they markedly increase postprandial hyperglycemia and hyperinsulinemia. Many high-carbohydrate foods common to Western diets produce a high glycemic response [high-glycemic-index (GI) foods], promoting postprandial carbohydrate oxidation at the expense of fat oxidation, thus altering fuel partitioning in a way that may be conducive to body fat gain. In contrast, diets based on low-fat foods that produce a low glycemic response (low-GI foods) may enhance weight control because they promote satiety, minimize postprandial insulin secretion, and maintain insulin sensitivity. This hypothesis is supported by several intervention studies in humans in which energy-restricted diets based on low-GI foods produced greater weight loss than did equivalent diets based on high-GI foods. Long-term studies in animal models have also shown that diets based on high-GI starches promote weight gain, visceral adiposity, and higher concentrations of lipogenic enzymes than do isoenergetic, macronutrient-controlled, low-GI-starch diets. In a study of healthy pregnant women, a high-GI diet was associated with greater weight at term than was a nutrient-balanced, low-GI diet. In a study of diet and complications of type 1 diabetes, the GI of the overall diet was an independent predictor of waist circumference in men. These findings provide the scientific rationale to justify randomized, controlled, multicenter intervention studies comparing the effects of conventional and low-GI diets on weight control.

PMID: 12081852 [PubMed - indexed for MEDLINE]

FASEB J. 1999 Nov;13(14):2051-60. [Links](#)

Markers of capacity to utilize fatty acids in human skeletal muscle: relation to insulin resistance and obesity and effects of weight loss.

[Simoneau JA](#),
[Veerkamp JH](#),
[Turcotte LP](#),
[Kelley DE](#).

Division of Kinesiology, Department of Social and Preventive Medicine, Faculty of Medicine, Laval University, Ste-Foy, Quebec.

A number of biochemical defects have been identified in glucose metabolism within skeletal muscle in obesity, and positive effects of weight loss on insulin resistance are also well established. Less is known about the capacity of skeletal muscle for the metabolism of fatty acids in obesity-related insulin resistance and of the effects of weight loss, though it is evident that muscle contains increased triglyceride. The current study was therefore undertaken to profile markers of human skeletal muscle for fatty acid metabolism in relation to obesity, in relation to the phenotype of insulin-resistant glucose metabolism, and to examine the effects of weight loss. Fifty-five men and women, lean and obese, with normal glucose tolerance underwent percutaneous biopsy of vastus lateralis skeletal muscle for determination of HADH, CPT, heparin-releasable (Hr) and tissue-extractable (Ext) LPL, CS, COX, PFK, and GAPDH enzyme activities, and content of cytosolic and plasma membrane FABP. Insulin sensitivity was measured using the euglycemic clamp method. DEXA was used to measure FM and FFM. In skeletal muscle of obese individuals, CPT, CS, and COX activities were lower while, conversely, they had a higher or similar content of FABP(C) and FABP(PM) than in lean individuals. Hr and Ext LPL activities were similar in both groups. In multivariate and simple regression analyses, there were significant correlations between insulin resistance and several markers of FA metabolism, notably, CPT and FABP(PM). These data suggest that in obesity-related insulin resistance, the metabolic capacity of skeletal muscle appears to be organized toward fat esterification rather than oxidation and that dietary-induced weight loss does not correct this disposition.

PMID: 10544188 [PubMed - indexed for MEDLINE]

J Clin Endocrinol Metab. 2000 Mar;85(3):1087-94. [Links](#)

Energy expenditure, fat oxidation, and body weight regulation: a study of metabolic adaptation to long-term weight change.

[Weyer C](#),
[Pratley RE](#),
[Salbe AD](#),
[Bogardus C](#),
[Ravussin E](#),
[Tataranni PA](#).

Clinical Diabetes and Nutrition Section, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Phoenix, Arizona 85016, USA.
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Relatively low rates of energy expenditure and fat oxidation predict body weight gain. Weight gain, in turn, is associated with increases in energy expenditure and fat oxidation that may oppose further weight change. In response to experimental weight gain induced by overfeeding, increases in energy expenditure and fat oxidation are overcompensatory, i.e. greater than predicted for the change in body composition. To determine whether such

metabolic adaptation occurs in response to spontaneous long term weight change, we conducted a longitudinal study in which 24-h energy expenditure (24-EE) and 24-h respiratory quotient (24-RQ; i.e. fat to carbohydrate oxidation) were repeatedly measured in 102 Pima Indians at baseline and after a mean follow-up of 3.6 +/- 2.7 yr, during which changes in body weight varied widely (-21 to +28 kg). We found that changes in 24-EE and 24-RQ in response to weight change were related to the amount of weight change, even after adjustment for body composition (partial $r = 0.23$ and -0.30 , respectively; both $P < 0.05$). For a 15-kg weight gain, the increases in 24-EE (+244 Cal/day) and 24-h fat oxidation (+152 Cal/day) were 33 and 53 Cal/day greater than predicted from the cross-sectional relationship between both measures and body weight. Changes in 24-EE and 24-RQ varied substantially among individuals. Thus, on the average, spontaneous long term weight changes are accompanied by small metabolic adaptations in both energy expenditure and fat oxidation. The metabolic responses to weight changes are highly variable among individuals, however. PMID: 10720044 [PubMed - indexed for MEDLINE]

Short-term Responses to high- and low GI Foods

- Lower decrease of serum leptin with HGI diet
 - Insulin acts as a leptin secretagogue
 - HGI foods lead to an increased intracellular glucose metabolism and an increased lipogenesis
 - Activation of hexosamine biosynthetic pathway leads to increased insulin resistance and serum leptin
- Probable functional improvement of leptin resistance associated with obesity might explain why albeit lower energy intakes with LGI foods satiety levels are higher
- REE decreases to a lesser extent with the LGI than with the HGI diet
 - Protein content of the diet?
 - Sleeping metabolic rate decreases more rapidly with a low-protein compared with a high-protein diet
 - Set point theory?
- Nitrogen balance is positive with a LGI diet and negative with a HGI diet
 - Counterregulatory hormones (e.g. cortisol) may have proteolytic actions

Agus MS et al Am J Clin Nutr 2000;71:901-7
 Wang J et al Nature. 1998 Jun 18;393(6686):684-8
 Gelfand RA et al J Clin Invest. 1984 Dec;74(6):2238-48
 Howe et al J Nutr. 1996 Sep;126(9):2120-9 Dr. C.P. Davis

Am J Clin Nutr. 2000 Apr;71(4):901-7. [Links](#)

Dietary composition and physiologic adaptations to energy restriction.

Agus MS,
Swain JF,
Larson CL,
Eckert EA,
Ludwig DS.

Division of Endocrinology, Department of Medicine, Children's Hospital, Boston, and the General Clinical Research Center, Brigham and Women's Hospital, Boston, MA 02115, USA. **BACKGROUND:** The concept of a body weight set point, determined predominantly by genetic mechanisms, has been proposed to explain the poor long-term results of conventional energy-restricted diets in the treatment of obesity. **OBJECTIVE:** The objective of this study was to examine whether dietary composition affects hormonal and metabolic adaptations to energy restriction. **DESIGN:** A randomized, crossover design was used to compare the effects of a high-glycemic-index (high-GI) and a low-glycemic-index (low-GI) energy-restricted diet.

The macronutrient composition of the high-GI diet was (as percent of energy) 67% carbohydrate, 15% protein, and 18% fat and that of the low-GI diet was 43% carbohydrate, 27% protein, and 30% fat; the diets had similar total energy, energy density, and fiber contents. The subjects, 10 moderately overweight young men, were studied for 9 d on 2 separate occasions. On days -1 to 0, they consumed self-selected foods ad libitum. On days 1-6, they received an energy-restricted high- or low-GI diet. On days 7-8, the high- or low-GI diets were consumed ad libitum. RESULTS: Serum leptin decreased to a lesser extent from day 0 to day 6 with the high-GI diet than with the low-GI diet. Resting energy expenditure declined by 10.5% during the high-GI diet but by only 4.6% during the low-GI diet (7.38 +/- 0.39 and 7.78 +/- 0.36 MJ/d, respectively, on days 5-6; P = 0.04). Nitrogen balance tended to be more negative, and energy intake from snacks on days 7-8 was greater, with the high-GI than the low-GI diet. CONCLUSION: Diets with identical energy contents can have different effects on leptin concentrations, energy expenditure, voluntary food intake, and nitrogen balance, suggesting that the physiologic adaptations to energy restriction can be modified by dietary composition.

PMID: 10731495 [PubMed - indexed for MEDLINE]

Nature. 1998 Jun 18;393(6686):684-8.[Related Articles](#), [Links](#)

A nutrient-sensing pathway regulates leptin gene expression in muscle and fat.

[Wang J](#), [Liu R](#), [Hawkins M](#), [Barzilai N](#), [Rossetti L](#).

Diabetes Research and Training Center, Albert Einstein College of Medicine, Bronx, New York 10461, USA.

Leptin, the protein encoded by the obese (ob) gene, is synthesized and released in response to increased energy storage in adipose tissue. However, it is still not known how incoming energy is sensed and transduced into increased expression of the ob gene. The hexosamine biosynthetic pathway is a cellular 'sensor' of energy availability and mediates the effects of glucose on the expression of several gene products. Here we provide evidence for rapid activation of ob gene expression in skeletal muscle by glucosamine. Increased tissue concentrations of the end product of the hexosamine biosynthetic pathway, UDP-N-acetylglucosamine (UDP-GlcNAc), result in rapid and marked increases in leptin messenger RNA and protein levels (although these levels were much lower than those in fat). Plasma leptin levels and leptin mRNA and protein levels in adipose tissue also increase. Most important, stimulation of leptin synthesis is reproduced by either hyperglycaemia or hyperlipidaemia, which also increase tissue levels of UDP-N-acetylglucosamine in conscious rodents. Finally, incubation of 3T3-L1 pre-adipocytes and L6 myocytes with glucosamine rapidly induces ob gene expression. Our findings are the first evidence of inducible leptin expression in skeletal muscle and unveil an important biochemical link between increased availability of nutrients and leptin expression.

Publication Types:

Research Support, Non-U.S. Gov't

Research Support, U.S. Gov't, P.H.S.

PMID: 9641678 [PubMed - indexed for MEDLINE]

J Clin Invest. 1984 Dec;74(6):2238-48.[Related Articles](#), [Links](#)

Role of counterregulatory hormones in the catabolic response to stress.

[Gelfand RA](#), [Matthews DE](#), [Bier DM](#), [Sherwin RS](#).

Patients with major injury or illness develop protein wasting, hypermetabolism, and hyperglycemia with increased glucose flux. To assess the role of elevated counterregulatory hormones in this response, we simultaneously infused cortisol (6 mg/m² per h), glucagon (4 ng/kg per min), epinephrine (0.6 microgram/m² per min), and norepinephrine (0.8 micrograms/m² per min) for 72 h into five obese subjects receiving only intravenous glucose (150 g/d). Four obese subjects received cortisol alone under identical conditions. Combined infusion maintained plasma hormone elevations typical of severe stress for 3 d. This caused a sustained increase in plasma glucose (60-80%), glucose production (100%), and total glucose flux (40%), despite persistent hyperinsulinemia. In contrast, resting metabolic rate changed little (9% rise, P = NS). Urinary nitrogen excretion promptly doubled and remained increased by approximately 4 g/d, reflecting increased excretion of urea and ammonia. Virtually all plasma amino acids declined. The increment in nitrogen excretion was similar in three additional combined infusion studies performed in 3-d fasted subjects not receiving glucose. Cortisol alone produced a smaller glycemic response (20-25%), an initially smaller insulin response, and a delayed rise in nitrogen excretion. By day 3, however, daily nitrogen excretion was equal to the combined group as was the elevation in plasma insulin. Most plasma amino acids rose rather than fell. In both infusion protocols nitrogen wasting was accompanied by only modest increments in 3-methylhistidine excretion (approximately 20-30%) and no significant change in leucine flux. We conclude: (a) Prolonged elevations of multiple stress hormones cause persistent hyperglycemia, increased glucose turnover, and increased nitrogen loss; (b) The sustained nitrogen loss is no greater than that produced by cortisol alone; (c) Glucagon, epinephrine, and norepinephrine transiently augment cortisol-induced nitrogen loss and persistently accentuate hyperglycemia; (d) Counterregulatory hormones contribute to, but are probably not the sole mediators of the massive nitrogen loss, muscle proteolysis, and hypermetabolism seen in some clinical settings of severe stress.

Publication Types:

Research Support, U.S. Gov't, P.H.S.

PMID: 6511925 [PubMed - indexed for MEDLINE]

J Nutr. 1996 Sep;126(9):2120-9.[Related Articles](#), [Links](#)

Dietary starch composition and level of energy intake alter nutrient oxidation in "carbohydrate-sensitive" men.

[Howe JC](#), [Rumpler WV](#), [Behall KM](#).

Energy and Protein Nutrition Laboratory and Carbohydrate Nutrition Laboratory, Beltsville Human Nutrition Research Center, U.S. Department of Agriculture, MD 20705, USA.

The effect of dietary starch type on components of 24-h energy expenditure (total, sleep, exercise) were examined in 13 hyperinsulinemic and nine control men, aged 28-58 y. Subjects consumed products containing 70% amylopectin or 70% amylose cornstarch for two 14-wk periods in a crossover design. A 10-wk period of starch replacement in the subjects' self-selected diets was followed by a 4-wk controlled feeding period at 100% maintenance energy

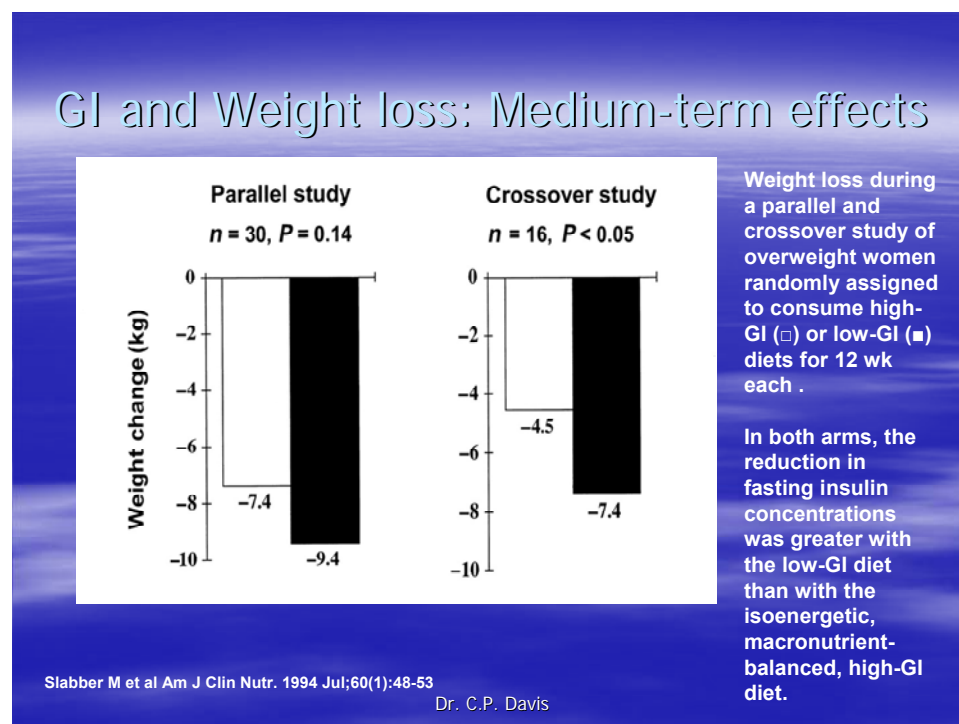
intake; diets during the last 4 d of the controlled feeding period provided excess energy, i.e., 125% of maintenance energy. Data for insulin, glucose, 24-h energy expenditure and its components, respiratory quotient and nutrient oxidation were analyzed by ANOVA for mixed models. Although insulin and glucose responses to a starch tolerance test remained greater for hyperinsulinemic than for control subjects, both were reduced with high amylose consumption ($P < 0.04$). No component of energy expenditure was significantly affected by dietary starch or subject type. However, excess energy intake did increase metabolic energy expenditure ($P < 0.0001$). Protein oxidation increased with excess energy intake when subjects consumed the high amylopectin starch but did not increase in response to excess energy consumption when the high amylose diet was consumed, suggesting increased protein retention. The magnitude of the response in carbohydrate and fat oxidation was blunted in hyperinsulinemic subjects consuming excess levels of the amylose diet. This may be due to an improvement in overall insulin response or to a change in available substrates for oxidation resulting from microbial fermentation.

Publication Types:

Clinical Trial

Randomized Controlled Trial

PMID: 8814200 [PubMed - indexed for MEDLINE]



Am J Clin Nutr. 1994 Jul;60(1):48-53. Links

Effects of a low-insulin-response, energy-restricted diet on weight loss and plasma insulin concentrations in hyperinsulinemic obese females.

[Slabber M](#),

[Barnard HC](#),

[Kuyl JM](#),

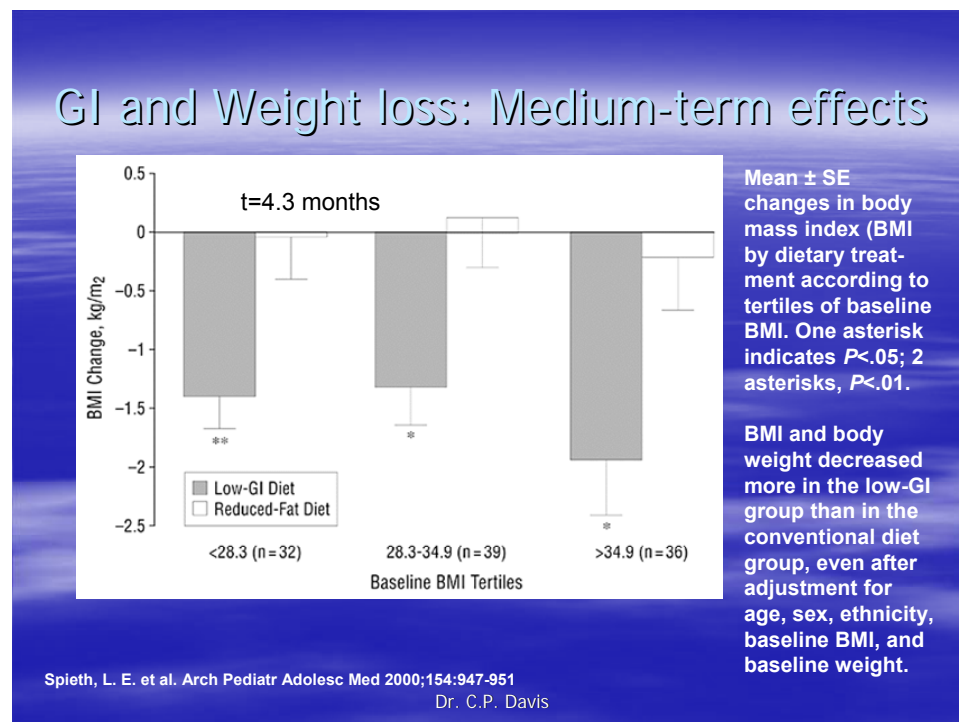
[Dannhauser A](#),

[Schall R](#).

Department of Human Nutrition, University of the Orange Free State, Bloemfontein, South Africa.

The effects of two low-energy diets on serum insulin concentrations and weight loss in obese hyperinsulinemic females were compared during a 12-wk period. The first diet (n = 15) was designed to evoke a low insulin response (ID), and the second (n = 15) was a conventionally balanced diet (ND). After a 12-wk washout period, seven and nine subjects who had been on the ID and ND, respectively, changed to the alternative diet for 12 wk. Variables studied were basal and 30- and 120-min concentrations of blood glucose, insulin, and C-peptide after an oral glucose load; body weight; and energy intake. Mean (\pm SD) weight was significantly reduced after ID and ND (9.35 \pm 2.49 and 7.41 \pm 4.23, respectively). The mean weight loss was more after ID. Fasting insulin concentrations decreased more after ID compared with ND (91.3 \pm 61.8 vs 21.0 \pm 71.5 pmol/L; $P < 0.05$). We conclude that ID significantly reduces serum insulin concentrations and weight in obese hyperinsulinemic females.

PMID: 8017337 [PubMed - indexed for MEDLINE]



Arch Pediatr Adolesc Med. 2000 Sep;154(9):947-51. Links

A low-glycemic index diet in the treatment of pediatric obesity.

[Spieth LE](#),
[Harnish JD](#),
[Lenders CM](#),
[Raezer LB](#),
[Pereira MA](#),
[Hangen SJ](#),
[Ludwig DS](#).

Department of Medicine, Children's Hospital, 300 Longwood Ave, Boston, MA 02115, USA.

CONTEXT: Conventional dietary approaches for the treatment of obesity have generally yielded disappointing results. OBJECTIVE: To examine the effects of a low-glycemic index (GI) diet compared with a standard reduced-fat diet in the management of pediatric obesity.

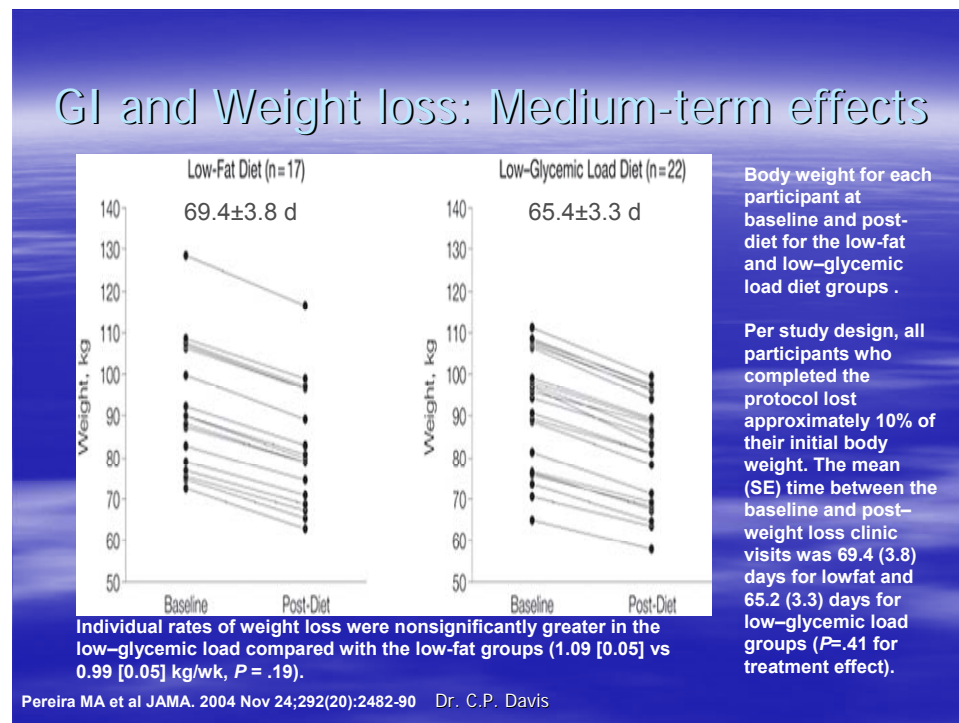
DESIGN: Retrospective cohort study of children attending an outpatient pediatric obesity program from September 1997 to December 1998. SETTING: Academic medical center.

PARTICIPANTS: One hundred seven obese but otherwise healthy children. MAIN

OUTCOME MEASURES: Changes in body mass index (BMI [calculated as weight in

kilograms divided by the square of height in meters]) and body weight from first to last clinic visit. RESULTS: A total of 64 patients received the low glycemic index diet and 43 received the reduced-fat diet for 4.3 vs 4.2 months' mean duration of follow-up, with 3.3 vs 3.3 mean number of visits, respectively. Body mass index (-1.53 kg/m²) [95% confidence interval, -1.94 to -1.12] vs -0.06 kg/m² [-0.56 to +0.44], P<.001) and body weight (-2.03 kg [95% confidence interval -3.19 to -0.88] vs +1.31 kg [-0.11 to +2.72], P<.001) decreased more in the low-GI group compared with the reduced-fat group. In multivariate models, these differences remained significant (P<.01) after adjustment for age, sex, ethnicity, BMI or baseline weight, participation in behavioral modification sessions, and treatment duration. Significantly more patients in the low-GI group experienced a decrease in BMI of at least 3 kg/m² (11 kg/m²) [17.2%] vs. 1 kg/m² [2.3%], P=.03). CONCLUSIONS: A low-GI diet seems to be a promising alternative to standard dietary treatment for obesity in children. Long-term randomized controlled trials of a low-GI diet in the prevention and treatment of obesity are needed.

PMID: 10980801 [PubMed - indexed for MEDLINE]



JAMA. 2004 Nov 24;292(20):2482-90. Links

Comment in:

[JAMA. 2005 Mar 9;293\(10\):1189; auhor reply 1189-90.](#)

Effects of a low-glycemic load diet on resting energy expenditure and heart disease risk factors during weight loss.

[Pereira MA](#),

[Swain J](#),

[Goldfine AB](#),

[Rifai N](#),

[Ludwig DS](#).

Department of Medicine, Children's Hospital, Boston, Mass 02115, USA.

CONTEXT: Weight loss elicits physiological adaptations relating to energy intake and expenditure that antagonize ongoing weight loss. OBJECTIVE: To test whether dietary composition affects the physiological adaptations to weight loss, as assessed by resting energy

expenditure. DESIGN, STUDY, AND PARTICIPANTS: A randomized parallel-design study of 39 overweight or obese young adults aged 18 to 40 years who received an energy-restricted diet, either low-glycemic load or low-fat. Participants were studied in the General Clinical Research Centers of the Brigham and Women's Hospital and the Children's Hospital, Boston, Mass, before and after 10% weight loss. The study was conducted from January 4, 2001, to May 6, 2003. MAIN OUTCOME MEASURES: Resting energy expenditure measured in the fasting state by indirect calorimetry, body composition by dual-energy x-ray absorptiometry, cardiovascular disease risk factors, and self-reported hunger. RESULTS: Resting energy expenditure decreased less with the low-glycemic load diet than with the low-fat diet, expressed in absolute terms (mean [SE], 96 [24] vs 176 [27] kcal/d; $P = .04$) or as a proportion (5.9% [1.5%] vs 10.6% [1.7%]; $P = .05$). Participants receiving the low-glycemic load diet reported less hunger than those receiving the low-fat diet ($P = .04$). Insulin resistance ($P = .01$), serum triglycerides ($P = .01$), C-reactive protein ($P = .03$), and blood pressure ($P = .07$ for both systolic and diastolic) improved more with the low-glycemic load diet. Changes in body composition (fat and lean mass) in both groups were very similar ($P = .85$ and $P = .45$, respectively). CONCLUSIONS: Changes in dietary composition within prevailing norms can affect physiological adaptations that defend body weight. Reduction in glycemic load may aid in the prevention or treatment of obesity, cardiovascular disease, and diabetes mellitus. PMID: 15562127 [PubMed - indexed for MEDLINE]

GI and Weight loss: Medium-term effects

	HGI diet		LGI diet	
	Baseline	5 Weeks	Baseline	5 Weeks
Total cholesterol				
Fasting (0 min; mmol/l)	5.52 ± 0.42	5.30 ± 0.39	5.30 ± 0.27	4.90 ± 0.38#
Morning AUC (mmol/min)	886 ± 61	824 ± 55	845 ± 47	762 ± 55†
Afternoon AUC (mmol/min)	897 ± 68	782 ± 0	874 ± 61	768 ± 57
Triacylglycerols				
Fasting (0 min; mmol/l)	1.33 ± 0.15	1.37 ± 0.22	1.59 ± 0.25	1.50 ± 0.42
Morning AUC (mmol · l ⁻¹ · 4 h ⁻¹)	292 ± 40	272 ± 47	336 ± 38	336 ± 62
Afternoon AUC (mmol · l ⁻¹ · 4 h ⁻¹)	334 ± 43	376 ± 55	413 ± 49	335 ± 36†*
FFA (0 min; mmol/l)	0.31 ± 0.02	0.32 ± 0.04	0.32 ± 0.03	0.39 ± 0.06
HDL cholesterol (mmol/l)	1.06 ± 0.09	1.06 ± 0.01	0.98 ± 0.08	1.01 ± 0.08
LDL cholesterol (mmol/l)§	4.01 ± 0.26	3.74 ± 0.21	3.71 ± 0.16	3.35 ± 0.32
ApoA (g/l)	1.5 ± 0.09	1.45 ± 0.08	1.45 ± 0.08	1.44 ± 0.09
ApoB (g/l)	1.28 ± 0.08	1.2 ± 0.07	1.21 ± 0.07	1.14 ± 0.06†
Total fat mass (kg)	19.54 ± 1.52	19.52 ± 1.57	19.27 ± 1.69	18.75 ± 1.59†*
Trunk fat (kg)	9.32 ± 0.86	8.92 ± 0.88	8.70 ± 0.93	8.41 ± 0.86†**

Five weeks of the LGI diet, compared with the same period of the HGI diet, induced a reduction of 700 g of total fat mass for eight subjects and >1 kg for five subjects. During the LGI diet, there was a gain of 430 ± 143 g of lean mass.

Bouche C et al Diabetes Care. 2002 May;25(5):822-8

Dr. C.P. Davis

Diabetes Care. 2002 May;25(5):822-8. [Links](#)

Five-week, low-glycemic index diet decreases total fat mass and improves plasma lipid profile in moderately overweight nondiabetic men.

[Bouche C](#),
[Rizkalla SW](#),
[Luo J](#),
[Vidal H](#),
[Veronese A](#),
[Pacher N](#),
[Fouquet C](#),

**Lang V,
Slama G.**

Institut National de la Sante et de la Recherche Medicale (INSERM) Unit 341, Department of Diabetes, AP Hotel-Dieu Hospital, Paris, France.

OBJECTIVE: To evaluate whether a 5-week low-glycemic index (LGI) diet versus a high-glycemic index (HGI) diet can modify glucose and lipid metabolism as well as total fat mass in nondiabetic men. **RESEARCH DESIGN AND METHODS:** In this study, 11 healthy men were randomly allocated to 5 weeks of an LGI or HGI diet separated by a 5-week washout interval in a crossover design. **RESULTS:** The LGI diet resulted in lower postprandial plasma glucose and insulin profiles and areas under the curve (AUCs) than the HGI diet. A 5-week period of the LGI diet lowered plasma triacylglycerol excursion after lunch (AUC, $P < 0.05$ LGI vs. HGI). These modifications were associated with a decrease in the total fat mass by approximately 700 g ($P < 0.05$) and a tendency to increase lean body mass ($P < 0.07$) without any change in body weight. This decrease in fat mass was accompanied by a decrease in leptin, lipoprotein lipase, and hormone-sensitive lipase RNA quantities in the subcutaneous abdominal adipose tissue ($P < 0.05$). **CONCLUSIONS:** We concluded that 5 weeks of an LGI diet ameliorates some plasma lipid parameters, decreases total fat mass, and tends to increase lean body mass without changing body weight. These changes were accompanied by a decrease in the expression of some genes implicated in lipid metabolism. Such a diet could be of benefit to healthy, slightly overweight subjects and might play a role in the prevention of metabolic diseases and their cardiovascular complications.

PMID: 11978675 [PubMed - indexed for MEDLINE]

GI and Weight loss: Medium-term effects

Table 2. Target and Actual Macronutrient Energy Distribution, Glycemic Index (GI), and Glycemic Load (GL)*

Variable	Diet 1		Diet 2		Diet 3		Diet 4		P Value†
	Target	Actual	Target	Actual	Target	Actual	Target	Actual	
CHO, % E	55	60 ± 1	55	56 ± 1	45	42 ± 1	45	40 ± 2	<.001
Protein, % E	15	18 ± 1	15	19 ± 0	25	28 ± 1	25	26 ± 1	<.001
Fat, % E	30	19 ± 1	30	22 ± 1	30	27 ± 1	30	29 ± 1	<.001
Alcohol, % E	0	2 ± 1	0	3 ± 1	0	2 ± 1	0	3 ± 1	.81
GI	67	70 ± 1	40	45 ± 1	57	59 ± 1	34	44 ± 1	<.001
GL, g	127	129 ± 8	75	89 ± 5	87	75 ± 3	54	59 ± 4	<.001

Abbreviations: CHO, carbohydrate; % E, percentage of total energy intake.

*Diet 1, high-CHO/high-GI; diet 2, high-CHO/low-GI; diet 3, high-protein/high-GI; and diet 4, high-protein/low-GI. Target values were the calculated values from sample menus. Actual values, which are expressed as mean ± SE, were calculated from food diaries completed during weeks 4 and 8 of the intervention.

†P value for comparison of actual values among the 4 diets.

McMillan-Price J et al Arch Intern Med. 2006 Jul 24;166(14):1466-75

Dr. C.P. Davis

Arch Intern Med. 2006 Jul 24;166(14):1466-75. Links

Comment in:

[Arch Intern Med. 2006 Jul 24;166\(14\):1438-9.](#)

[Arch Intern Med. 2007 Jan 22;167\(2\):206; author reply 206-7.](#)

Comparison of 4 diets of varying glycemic load on weight loss and cardiovascular risk reduction in overweight and obese young adults: a randomized controlled trial.

[McMillan-Price J,](#)

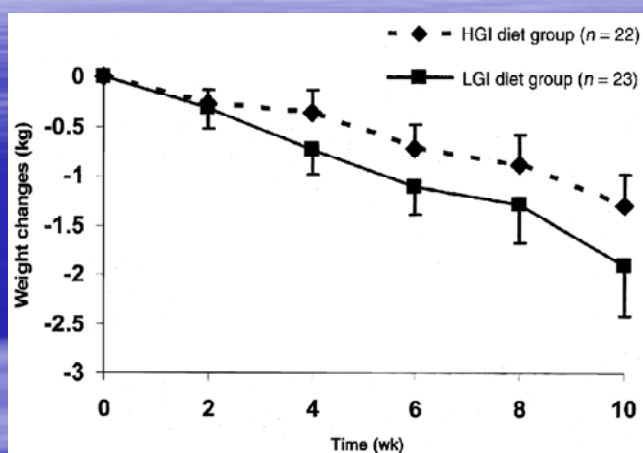
[Petocz P,](#)
[Atkinson F,](#)
[O'Neill K,](#)
[Samman S,](#)
[Steinbeck K,](#)
[Caterson I,](#)
[Brand-Miller J.](#)

Human Nutrition Unit, University of Sydney, Sydney, Australia.

BACKGROUND: Despite the popularity of low-glycemic index (GI) and high-protein diets, to our knowledge no randomized, controlled trials have systematically compared their relative effects on weight loss and cardiovascular risk. **METHODS:** A total of 129 overweight or obese young adults (body mass index, ≥ 25 [calculated as weight in kilograms divided by the square of height in meters]) were assigned to 1 of 4 reduced-fat, high-fiber diets for 12 weeks. Diets 1 and 2 were high carbohydrate (55% of total energy intake), with high and low GIs, respectively; diets 3 and 4 were high protein (25% of total energy intake), with high and low GIs, respectively. The glycemic load was highest in diet 1 and lowest in diet 4. Changes in weight, body composition, and blood chemistry profile were studied. **RESULTS:** While all groups lost a similar mean \pm SE percentage of weight (diet 1, $-4.2\% \pm 0.6\%$; diet 2, $-5.5\% \pm 0.5\%$; diet 3, $-6.2\% \pm 0.4\%$; and diet 4, $-4.8\% \pm 0.7\%$; $P = .09$), the proportion of subjects in each group who lost 5% or more of body weight varied significantly by diet (diet 1, 31%; diet 2, 56%; diet 3, 66%; and diet 4, 33%; $P = .01$). Women on diets 2 and 3 lost approximately 80% more fat mass (-4.5 ± 0.5 [mean \pm SE] kg and -4.6 ± 0.5 kg) than those on diet 1 (-2.5 ± 0.5 kg; $P = .007$). Mean \pm SE low-density-lipoprotein cholesterol levels declined significantly in the diet 2 group (-6.6 ± 3.9 mg/dL [-0.17 ± 0.10 mmol/L]) but increased in the diet 3 group ($+10.0 \pm 3.9$ mg/dL [$+0.26 \pm 0.10$ mmol/L]; $P = .02$). Goals for energy distribution were not achieved exactly: both carbohydrate groups ate less fat, and the diet 2 group ate more fiber. **CONCLUSION:** Both high-protein and low-GI regimens increase body fat loss, but cardiovascular risk reduction is optimized by a high-carbohydrate, low-GI diet.

PMID: 16864756 [PubMed - indexed for MEDLINE]

GI and Weight loss: Medium-term effects



Mean (\pm SEM) BW changes during 10 wk ad libitum intake of a HGI or a LGI diet in overweight women. diet, $P = 0.44$; time, $P = 0.001$.

There was no significant difference in BW changes between groups (LGI: -1.9 ± 0.5 kg; HGI: -1.3 ± 0.3 kg; $P = 0.31$), but body weight decreased significantly in both groups over time.

Am J Clin Nutr. 2004 Aug;80(2):337-47. Links

Comment in:

[Am J Clin Nutr. 2005 Apr;81\(4\):940-1; author reply 941.](#)

[Am J Clin Nutr. 2005 Mar;81\(3\):722-3; author reply 723-4.](#)

No difference in body weight decrease between a low-glycemic-index and a high-glycemic-index diet but reduced LDL cholesterol after 10-wk ad libitum intake of the low-glycemic-index diet.

[Sloth B,](#)

[Krog-Mikkelsen I,](#)

[Flint A,](#)

[Tetens I,](#)

[Bjorck I,](#)

[Vinoy S,](#)

[Elmstahl H,](#)

[Astrup A,](#)

[Lang V,](#)

[Raben A.](#)

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BACKGROUND: The role of glycemic index (GI) in appetite and body-weight regulation is still not clear. **OBJECTIVE:** The objective of the study was to investigate the long-term effects of a low-fat, high-carbohydrate diet with either low glycemic index (LGI) or high glycemic index (HGI) on ad libitum energy intake, body weight, and composition, as well as on risk factors for type 2 diabetes and ischemic heart disease in overweight healthy subjects. **DESIGN:** The study was a 10-wk parallel, randomized, intervention trial with 2 matched groups. The LGI or HGI test foods, given as replacements for the subjects' usual carbohydrate-rich foods, were equal in total energy, energy density, dietary fiber, and macronutrient composition. Subjects were 45 (LGI diet: $n = 23$; HGI diet: $n = 22$) healthy overweight [body mass index (in kg/m^2): 27.6 ± 0.2] women aged 20-40 y. **RESULTS:** Energy intake, mean (\pm SEM) body weight (LGI diet: -1.9 ± 0.5 kg; HGI diet: -1.3 ± 0.3 kg), and fat mass (LGI diet: -1.0 ± 0.4 kg; HGI diet: -0.4 ± 0.3 kg) decreased over time, but the differences between groups were not significant. No significant differences were observed between groups in fasting serum insulin, homeostasis model assessment for relative insulin resistance, homeostasis model assessment for beta cell function, triacylglycerol, nonesterified fatty acids, or HDL cholesterol. However, a 10% decrease in LDL cholesterol ($P < 0.05$) and a tendency to a larger decrease in total cholesterol ($P = 0.06$) were observed with consumption of the LGI diet as compared with the HGI diet. **CONCLUSIONS:** This study does not support the contention that low-fat LGI diets are more beneficial than HGI diets with regard to appetite or body-weight regulation as evaluated over 10 wk. However, it confirms previous findings of a beneficial effect of LGI diets on risk factors for ischemic heart disease. PMID: 15277154 [PubMed - indexed for MEDLINE]

Medium-term Responses to HGI- and LGI Foods

- Greater decrease of fasting and stimulated serum insulin with LGI diets
 - In a crossover study, serum insulin levels dropped significantly, whereas C-peptide levels remained stable indicating greater hepatic clearance of insulin with LGI. Only after 12 mo of continued weight loss and maintenance of that loss, there was a significant drop in insulin production with LGI.
 - Hypertrophic β -cells in obesity
- LGI-diets may improve plasma lipid profile and fat mass
 - Tendency to decrease fasting plasma total and LDL-cholesterol and increase HDL-cholesterol
 - Dietary fibers bind cholesterol and may have an influence on plasma lipid profile
 - Tendency to decreased postprandial triacylglycerol excursion

Slabber M et al Am J Clin Nutr. 1994 Jul;60(1):48-53
Wee et al Med Sci Sports Exerc. 1999 Mar;31(3):393-9
Boivin A et al Am J Physiol. 1994 Oct;267(4 Pt 1):E620-7

Dr. C.P. Davis

Am J Clin Nutr. 1994 Jul;60(1):48-53. [Links](#)

Effects of a low-insulin-response, energy-restricted diet on weight loss and plasma insulin concentrations in hyperinsulinemic obese females.

Slabber M,
Barnard HC,
Kuyl JM,
Dannhauser A,
Schall R.

Department of Human Nutrition, University of the Orange Free State, Bloemfontein, South Africa.

The effects of two low-energy diets on serum insulin concentrations and weight loss in obese hyperinsulinemic females were compared during a 12-wk period. The first diet (n = 15) was designed to evoke a low insulin response (ID), and the second (n = 15) was a conventionally balanced diet (ND). After a 12-wk washout period, seven and nine subjects who had been on the ID and ND, respectively, changed to the alternative diet for 12 wk. Variables studied were basal and 30- and 120-min concentrations of blood glucose, insulin, and C-peptide after an oral glucose load; body weight; and energy intake. Mean (\pm SD) weight was significantly reduced after ID and ND (9.35 \pm 2.49 and 7.41 \pm 4.23, respectively). The mean weight loss was more after ID. Fasting insulin concentrations decreased more after ID compared with ND (91.3 \pm 61.8 vs 21.0 \pm 71.5 pmol/L; $P < 0.05$). We conclude that ID significantly reduces serum insulin concentrations and weight in obese hyperinsulinemic females.

PMID: 8017337 [PubMed - indexed for MEDLINE]

Med Sci Sports Exerc. 1999 Mar;31(3):393-9. [Related Articles](#). [Links](#)

- Influence of high and low glycemic index meals on endurance running capacity.

[Wee SL](#), [Williams C](#), [Gray S](#), [Horabin J](#).

Department of Physical Education, Sports Science and Recreation Management,
Loughborough University, Leicestershire, United Kingdom.

PURPOSE: The purpose of this study was to examine the effect of high and low glycemic index (GI) carbohydrate (CHO) pre-exercise meals on endurance running capacity.

METHODS: Eight active subjects (five male and three female) ran on a treadmill at approximately 70% VO₂max to exhaustion on two occasions separated by 7 d. Three hours before the run after an overnight fast, each subject was given in a single-blind, random order, isoenergetic meal of 850 \pm 21 kcal (mean \pm SEM; 67% carbohydrate, 30% protein, and 3% fat) containing either high (HGI) or low (LGI) GI carbohydrate foods providing 2.0 g CHO.kg⁻¹ body weight. **RESULTS:** Ingestion of the HGI meal resulted in a 580% and 330% greater incremental area under the 3-h blood glucose and serum insulin response curves, respectively. Performance times were not different between the HGI and LGI trials (113 \pm 4 min and 111 \pm 5 min, respectively). During the first 80 min of exercise in the LGI trial, CHO oxidation was 12% lower and fat oxidation was 118% higher than in the HGI trial. Although serum insulin concentrations did not differ between trials, blood glucose at 20 min into exercise in the HGI trial was lower than that during the LGI trial at the same time (3.6 \pm 0.3 mmol.L⁻¹ vs 4.3 \pm 0.3 mmol.L⁻¹; P < 0.05). During exercise, plasma glycerol and serum free fatty acid concentrations were lower in the HGI trial than in the LGI trial.

CONCLUSIONS: This results demonstrate that although there is a relative shift in substrate utilization from CHO to fat when a low GI meal is ingested before exercise compared with that for a high GI meal, there is no difference in endurance running capacity.

Publication Types:

Clinical Trial

Randomized Controlled Trial

Research Support, Non-U.S. Gov't

PMID: 10188743 [PubMed - indexed for MEDLINE]

Am J Physiol. 1994 Oct;267(4 Pt 1):E620-7. [Links](#)

Postprandial modulation of lipoprotein lipase in rats with insulin resistance.

[Boivin A,](#)
[Montplaisir I,](#)
[Deshaies Y.](#)

Department of Physiology, School of Medicine, Laval University, Quebec, Canada.

The purpose of this study was to determine whether the postprandial modulation of lipoprotein lipase (LPL) activity was altered in rats with resistance of glucose metabolism to insulin action induced by a high-fat diet. Relationships between serum insulin and tissue LPL activity were established in rats chronically fed a high-carbohydrate or high-fat diet, and the effects of fasting and intake of meals of habitual and alternate composition were contrasted. The feeding paradigm did not result in the development of obesity. Global resistance of glucose metabolism to insulin brought about by chronic high-fat feeding was confirmed by an intravenous glucose tolerance test. Fasting serum glucose and insulin concentrations were similar in both cohorts, as was LPL activity in retroperitoneal and inguinal white adipose tissues (WAT), the heart, and soleus. A high-carbohydrate meal brought about higher postprandial insulinemia in the cohort chronically fed the high-fat diet. This was associated with larger changes in LPL activity, that is, an increase in inguinal WAT and in brown adipose tissue and a decrease in soleus, red vastus lateralis, and the heart. Thus the established postprandial modulation of LPL, presumably by insulin, was potentiated in the presence of hyperinsulinemia induced by chronic high-fat feeding despite the concomitant impairment of glucose metabolism.

Medium-term Responses to HGI- and LGI Foods

- LGI-diets may change body composition
 - Reduction of visceral fat pads
 - Difference in nitrogen balance and protein metabolism
 - Shift in substrate utilization
 - after an LGI test meal, carbohydrate oxidation was 12% lower and fat oxidation was 118% higher than after an HGI test meal
 - some proteins and genes specific to adipose tissue might be active in the regulation of fat mass by LGI diets
 - the LPL level in adipose tissue is positively correlated with insulinemia
 - A diet's glycemic effect influences fuel storage within the body
 - chronic consumption of high-GI diets, compared with nutrient-balanced low-GI diets, was associated with higher muscle glycogen (14%) and muscle triacylglycerol (22%) concentrations
 - Chronic hyperinsulinemia?
 - HGI meals result in an increased glycogen storage in muscle cells if eaten within in the first 24 hours after prolonged exercise
 - Activation of glycogen synthase by insulin
 - Immediate availability of HGI starches

Kiess B, Richter EA *Am J Clin Nutr.* 1996 Jan;63(1):47-53
Burke LM et al *Appl Physiol.* 1993 Aug;75(2):1019-23

Dr. C.P. Davis

Am J Clin Nutr. 1996 Jan;63(1):47-53. Links

Types of carbohydrate in an ordinary diet affect insulin action and muscle substrates in humans.

[Kiess B.](#)
[Richter EA.](#)

Copenhagen Muscle Research Center, August Krogh Institute, University of Copenhagen, Denmark.

The influence of dietary carbohydrate types on insulin action and muscle substrates was investigated. Seven healthy young men ingested two isoenergetic diets with 46-47% of energy as carbohydrates, 41% as fat, and 13-14% as protein, in which the carbohydrates either had a high glycemic index (HGI) or a low glycemic index (LGI) for 30 d, two times in a randomized crossover design. A euglycemic hyperinsulinemic clamp procedure was performed at the end of each dietary period. Whole-body glucose uptake was similar with both diets at a low plasma insulin concentration (370 pmol/L) but decreased ($P < 0.05$) at a high insulin concentration (2.4 nmol/L) with the LGI diet compared with the HGI diet. Higher plasma fatty acid concentrations during part of the day were found with the LGI diet compared with the HGI diet ($P < 0.05$). Initially, blood glucose and plasma insulin concentrations were lower ($P < 0.05$) during part of the day with the LGI than with the HGI diet, but after 30 d of the diet this difference diminished. Muscle glycogen and triacylglycerol concentrations were increased ($P < 0.05$) by 14% and 22%, respectively, with the HGI diet compared with the LGI diet, and muscle triacylglycerol concentrations did not correlate with insulin action. It is concluded that when ingesting a diet with an energy composition common in Western countries, switching the carbohydrates from high to low GI sources decreases insulin action on whole-body glucose disposal at a high but not at a physiologic plasma insulin concentration. Furthermore, adaptation in terms of carbohydrate digestion and/or absorption to a diet rich in LGI carbohydrates may take place over 4 wk.

PMID: 8604670 [PubMed - indexed for MEDLINE]

J Appl Physiol. 1993 Aug;75(2):1019-23. [Links](#)

Muscle glycogen storage after prolonged exercise: effect of the glycemic index of carbohydrate feedings.

[Burke LM](#),

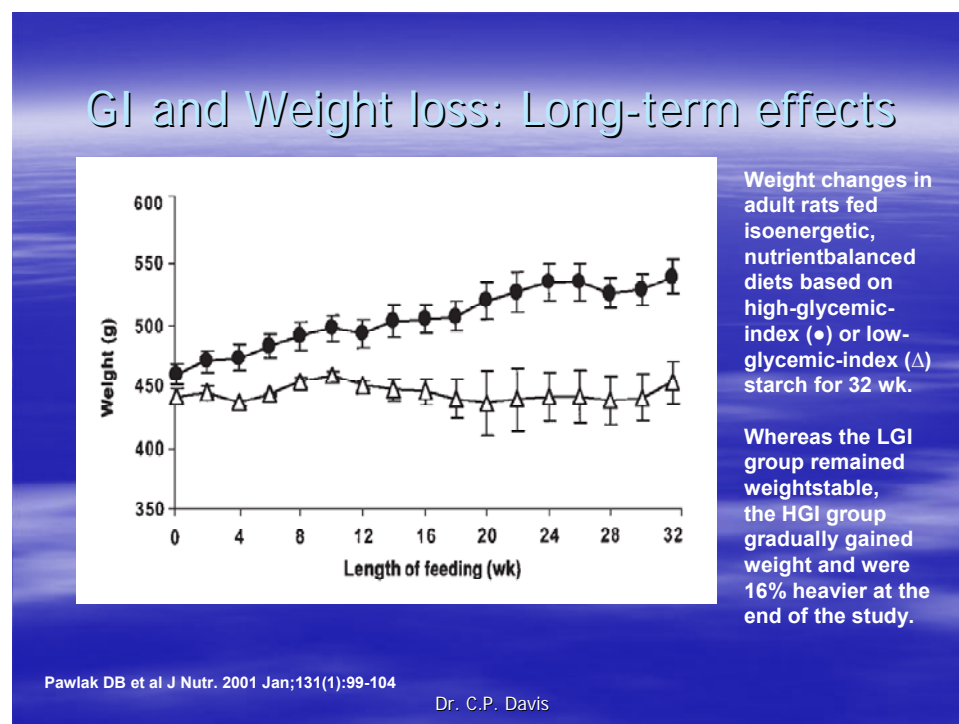
[Collier GR](#),

[Hargreaves M](#).

Department of Sports Medicine, Australian Institute of Sport, Australian Capital Territory.

The effect of the glycemic index (GI) of postexercise carbohydrate intake on muscle glycogen storage was investigated. Five well-trained cyclists undertook an exercise trial to deplete muscle glycogen (2 h at 75% of maximal O₂ uptake followed by four 30-s sprints) on two occasions, 1 wk apart. For 24 h after each trial, subjects rested and consumed a diet composed exclusively of high-carbohydrate foods, with one trial providing foods with a high GI (HI GI) and the other providing foods with a low GI (LO GI). Total carbohydrate intake over the 24 h was 10 g/kg of body mass, evenly distributed between meals eaten 0, 4, 8, and 21 h postexercise. Blood samples were drawn before exercise, immediately after exercise, immediately before each meal, and 30, 60, and 90 min post-prandially. Muscle biopsies were taken from the vastus lateralis immediately after exercise and after 24 h. When the effects of the immediate postexercise meal were excluded, the totals of the incremental glucose and insulin areas after each meal were greater ($P \leq 0.05$) for the HI GI meals than for the LO GI meals. The increase in muscle glycogen content after 24 h of recovery was greater ($P = 0.02$) with the HI GI diet (106 ± 11.7 mmol/kg wet wt) than with the LO GI diet (71.5 ± 6.5 mmol/kg). The results suggest that the most rapid increase in muscle glycogen content during the first 24 h of recovery is achieved by consuming foods with a high GI.

PMID: 8226443 [PubMed - indexed for MEDLINE]



J Nutr. 2001 Jan;131(1):99-104. [Links](#)

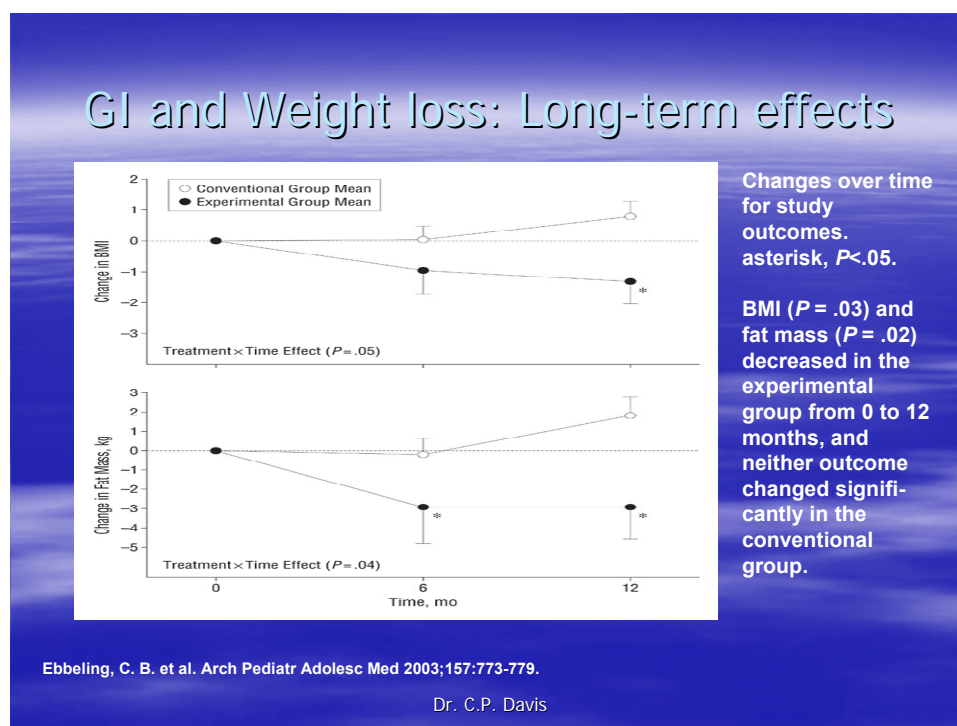
High glycemic index starch promotes hypersecretion of insulin and higher body fat in rats without affecting insulin sensitivity.

[Pawlak DB](#),
[Bryson JM](#),
[Denver GS](#),
[Brand-Miller JC](#).

Human Nutrition Unit, Department of Biochemistry, The University of Sydney, NSW 2006, Australia.

In rats, prolonged feeding of high glycemic index (GI) starch results in basal hyperinsulinemia and an elevated insulin response to an intravenous glucose tolerance test (IVGTT). The aim of this study was to assess hepatic and peripheral insulin resistance (IR) using euglycemic hyperinsulinemic clamps. Insulin sensitivity, epididymal fat deposition and fasting leptin concentrations were compared in rats fed isocalorically a low or high GI diet for 7 wk (45% carbohydrate, 35% fat and 20% protein as energy) or a high fat diet (20% carbohydrate, 59% fat and 21% protein as energy) for 4 wk so that final body weights were similar. At the end of the study, high GI rats had higher basal leptin concentration and epididymal fat mass than the low GI group, despite comparable body weights. High GI and high fat feeding both resulted in the higher insulin response during IVGTT, but impaired glucose tolerance was seen only in rats fed high fat. The GI of the diet did not affect basal and clamp glucose uptake or hepatic glucose output, but high fat feeding induced both peripheral and hepatic IR. The findings suggest that hypersecretion of insulin without IR may be one mechanism for increased fat deposition in rats fed high GI diets.

PMID: 11208944 [PubMed - indexed for MEDLINE]



Arch Pediatr Adolesc Med. 2003 Aug;157(8):773-9. Links
Comment in:

[Arch Pediatr Adolesc Med. 2003 Aug;157\(8\):725-7.](#)

A reduced-glycemic load diet in the treatment of adolescent obesity.

[Ebbeling CB](#),
[Leidig MM](#),
[Sinclair KB](#),
[Hangen JP](#),

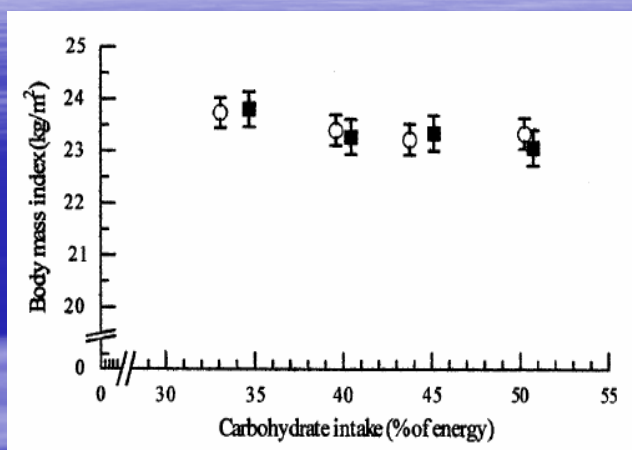
Ludwig DS.

Division of Endocrinology, Department of Medicine, Children's Hospital Boston, MA 02115, USA.

BACKGROUND: The incidence of type 2 diabetes increases markedly for obese children after puberty. However, the effect of dietary composition on body weight and diabetes risk factors has not been studied in adolescents. **OBJECTIVE:** To compare the effects of an ad libitum, reduced-glycemic load (GL) diet with those of an energy-restricted, reduced-fat diet in obese adolescents. **DESIGN:** Randomized control trial consisting of a 6-month intervention and a 6-month follow-up. **MAIN OUTCOME MEASURES:** Body composition (body mass index [BMI; calculated as weight in kilograms divided by the square of height in meters] and fat mass) and insulin resistance (homeostasis model assessment) were measured at 0, 6, and 12 months. Seven-day food diaries were used as a process measure. **SUBJECTS:** Sixteen obese adolescents aged 13 to 21 years. **Intervention Experimental (reduced-GL) treatment** emphasized selection of foods characterized by a low to moderate glycemic index, with 45% to 50% of energy from carbohydrates and 30% to 35% from fat. In contrast, **conventional (reduced-fat) treatment** emphasized selection of low-fat products, with 55% to 60% of energy from carbohydrates and 25% to 30% from fat. **RESULTS:** Fourteen subjects completed the study (7 per group). The GL decreased significantly in the experimental group, and dietary fat decreased significantly in the conventional group ($P < .05$ for both). At 12 months, mean \pm SEM BMI (-1.3 ± 0.7 vs 0.7 ± 0.5 ; $P = .02$) and fat mass (-3.0 ± 1.6 vs 1.8 ± 1.0 kg; $P = .01$) had decreased more in the experimental compared with the conventional group, differences that were materially unchanged in an intention-to-treat model ($n = 16$) (BMI, $P = .02$; fat mass, $P = .01$). Insulin resistance as measured by means of homeostasis model assessment increased less in the experimental group during the intervention period (-0.4 ± 0.9 vs 2.6 ± 1.2 ; $P = .02$). In post hoc analyses, GL was a significant predictor of treatment response among both groups ($R^2 = 0.51$; $P = .006$), whereas dietary fat was not ($R^2 = 0.14$; $P = .22$). **CONCLUSIONS:** An ad libitum reduced-GL diet appears to be a promising alternative to a conventional diet in obese adolescents. Large-scale randomized controlled trials are needed to further evaluate the effectiveness of reduced-GL and -glycemic index diets in the treatment of obesity and prevention of type 2 diabetes.

PMID: 12912783 [PubMed - indexed for MEDLINE]

GI and Weight loss: Epidemiologic Evidence



Adjusted mean BMI (95% CI) in quartiles of carbohydrate intake (percentage of energy) for 1043 males (○) and 1006 females (■) with type 1 diabetes.

In both men and women, higher intakes of carbohydrates were associated with a lower BMI.

Nutrient intakes as predictors of body weight in European people with type 1 diabetes.

[Toeller M](#),

[Buyken AE](#),

[Heitkamp G](#),

[Cathelineau G](#),

[Ferriss B](#),

[Michel G](#);

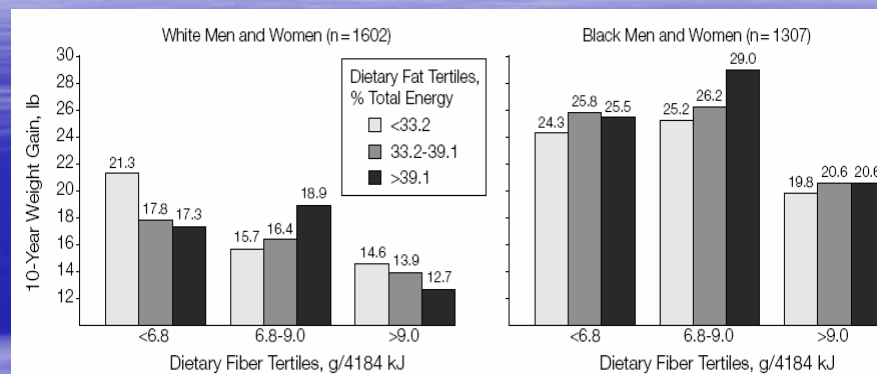
[EURODIAB IDDM Complications Study Group](#).

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BACKGROUND: Overweight and obesity are also found among persons with type 1 diabetes. **OBJECTIVE:** The present study examined which nutrients predict the body mass index (BMI), the waist-to-hip ratio (WHR) and the waist circumference (WC) of European persons with type 1 diabetes. **DESIGN:** Cross-sectional, clinic-based study (EURODIAB Complications Study). **SUBJECTS AND METHODS:** Nutrient intakes (assessed by a 3-day dietary record) predicting measures of body weight (BMI, WHR and WC) were determined by stepwise forward regression analysis in 1458 males and 1410 females with type 1 diabetes ($P < \text{or} = 0.05$ for inclusion). **RESULTS:** In men, a higher carbohydrate intake was a significant independent predictor for lower levels of BMI, WHR and WC, an increased saturated fat intake and a lower intake of cereal fibre predicted a higher WHR, a higher monounsaturated fat intake and a lower glycaemic index of the diet determined lower levels of WHR and WC, and a moderate consumption of alcohol determined an increased WC. In women, a higher carbohydrate intake predicted a lower BMI and a thinner WC, no alcohol consumption determined a lower BMI, and an increased intake of saturated fat and a lower consumption of cereal fibre were significant independent predictors for a higher WHR. **CONCLUSIONS:** A modified fat intake, an increase of carbohydrate and cereal fibre intake and a preferred consumption of low glycaemic index foods are independently related to lower measures of body weight in European persons with type 1 diabetes.

PMID: 11781763 [PubMed - indexed for MEDLINE]

GI and Weight loss: Epidemiologic Evidence



In the CARDIA study of young adults, low fiber consumption (GI was not assessed) predicted higher 10-y weight gain, waist-to-hip ratio, and 2-h postglucose insulin concentrations (a measure of insulin resistance) to a greater extent than did total or saturated fat consumption.

Ludwig, D. S. et al. JAMA 1999;282:1539-1546

Dr. C.P. Davis

JAMA. 1999 Oct 27;282(16):1539-46. Links

Comment in:

[JAMA. 2000 Apr 12;283\(14\):1821; author reply 1821-2.](#)

[JAMA. 2000 Apr 12;283\(14\):1821; author reply 1821-2.](#)

Dietary fiber, weight gain, and cardiovascular disease risk factors in young adults.

[Ludwig DS,](#)

[Pereira MA,](#)

[Kroenke CH,](#)

[Hilner JE,](#)

[Van Horn L,](#)

[Slattery ML,](#)

[Jacobs DR Jr.](#)

Department of Medicine, Children's Hospital, Boston, Mass 02115, USA.

CONTEXT: Dietary composition may affect insulin secretion, and high insulin levels, in turn, may increase the risk for cardiovascular disease (CVD). OBJECTIVE: To examine the role of fiber consumption and its association with insulin levels, weight gain, and other CVD risk factors compared with other major dietary components. DESIGN AND SETTING: The Coronary Artery Risk Development in Young Adults (CARDIA) Study, a multicenter population-based cohort study of the change in CVD risk factors over 10 years (1985-1986 to 1995-1996) in Birmingham, Ala; Chicago, Ill; Minneapolis, Minn; and Oakland, Calif.

PARTICIPANTS: A total of 2909 healthy black and white adults, 18 to 30 years of age at enrollment. MAIN OUTCOME MEASURES: Body weight, insulin levels, and other CVD risk factors at year 10, adjusted for baseline values. RESULTS: After adjustment for potential confounding factors, dietary fiber showed linear associations from lowest to highest quintiles of intake with the following: body weight (whites: 174.8-166.7 lb [78.3-75.0 kg], $P < .001$; blacks: 185.6-177.6 lb [83.5-79.9 kg], $P = .001$), waist-to-hip ratio (whites: 0.813-0.801, $P = .004$; blacks: 0.809-0.799, $P = .05$), fasting insulin adjusted for body mass index (whites: 77.8-72.2 pmol/L [11.2-10.4 microU/mL], $P = .007$; blacks: 92.4-82.6 pmol/L [13.3-11.9 microU/mL], $P = .01$) and 2-hour postglucose insulin adjusted for body mass index (whites: 261.1-234.7 pmol/L [37.6-33.8 microU/mL], $P = .03$; blacks: 370.2-259.7 pmol/L [53.3-37.4

microU/mL], $P < .001$). Fiber was also associated with blood pressure and levels of triglyceride, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and fibrinogen; these associations were substantially attenuated by adjustment for fasting insulin level. In comparison with fiber, intake of fat, carbohydrate, and protein had inconsistent or weak associations with all CVD risk factors. **CONCLUSIONS:** Fiber consumption predicted insulin levels, weight gain, and other CVD risk factors more strongly than did total or saturated fat consumption. High-fiber diets may protect against obesity and CVD by lowering insulin levels.

PMID: 10546693 [PubMed - indexed for MEDLINE]

A hypothetical Biochemical Scenario

- Consumption of a CHO, HGI diet results in recurrent postprandial hyperglycemia and hyperinsulinemia that is accentuated in sedentary persons who are overweight, insulinresistant, or both
 - Increased carbohydrate oxidation and decreased fat oxidation throughout the postprandial period, whether the person is at rest or exercising
 - The expression of enzymes involved in lipid synthesis is up-regulated, whereas the expression of those involved in lipid oxidation are down-regulated.
- Counterregulatory hormonal responses (eg, of cortisol and noradrenaline) are higher with HGI foods because of the hyperglycemic-hypoglycemic rebound after consumption
 - Stimulation of gluconeogenesis from gluconeogenic amino acids as well as meal initiation in free-feeding individuals. The 0–6-h period following consumption of a high-GI diet is therefore characterized by a greater dependence on carbohydrate and protein as sources of fuel and less dependence on fat. Because carbohydrate and protein stores are limited, their higher rate of usage may stimulate appetite and encourage overconsumption.
 - Small energy imbalances that are characteristic of modern lifestyles are more likely to promote gradual expansion of the fat stores (possibly at the expense of lean tissue) when the diet is based on high-GI foods.

Brand-Miller JC et al Am J Clin Nutr. 2002 Jul;76(1):281S-5S
Dr. C.P. Davis

Am J Clin Nutr. 2002 Jul;76(1):281S-5S. [Links](#)

Glycemic index and obesity.

[Brand-Miller JC](#),

[Holt SH](#),

[Pawlak DB](#),

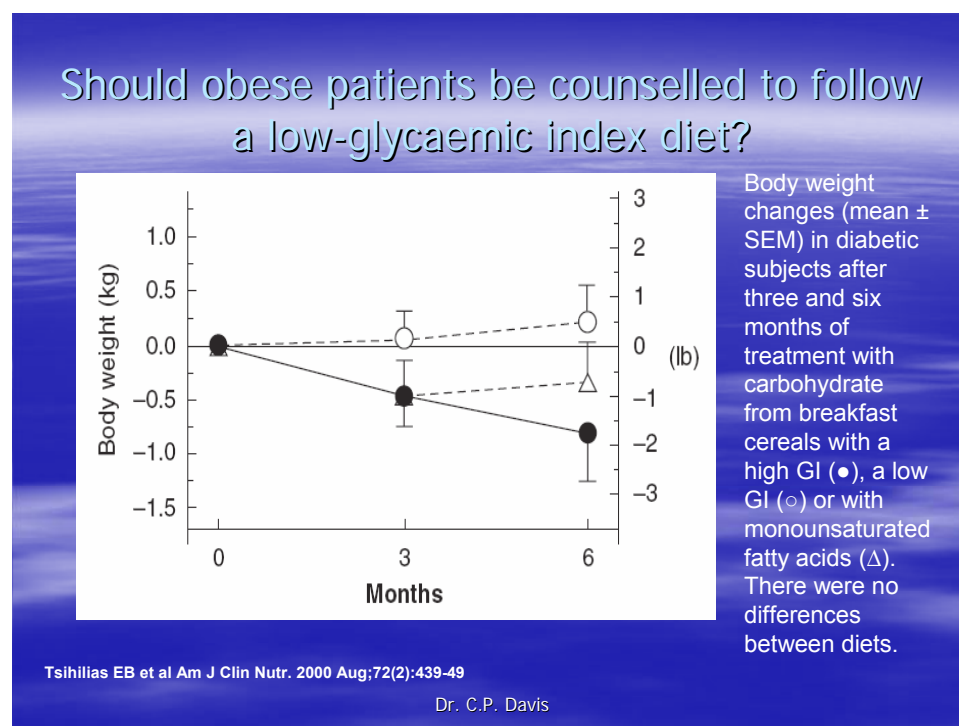
[McMillan J](#).

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Although weight loss can be achieved by any means of energy restriction, current dietary guidelines have not prevented weight regain or population-level increases in obesity and overweight. Many high-carbohydrate, low-fat diets may be counterproductive to weight control because they markedly increase postprandial hyperglycemia and hyperinsulinemia. Many high-carbohydrate foods common to Western diets produce a high glycemic response [high-glycemic-index (GI) foods], promoting postprandial carbohydrate oxidation at the expense of fat oxidation, thus altering fuel partitioning in a way that may be conducive to body fat gain. In contrast, diets based on low-fat foods that produce a low glycemic response (low-GI foods) may enhance weight control because they promote satiety, minimize postprandial insulin secretion, and maintain insulin sensitivity. This hypothesis is supported by several intervention studies in humans in which energy-restricted diets based on low-GI foods produced greater weight loss than did equivalent diets based on high-GI foods. Long-

term studies in animal models have also shown that diets based on high-GI starches promote weight gain, visceral adiposity, and higher concentrations of lipogenic enzymes than do isoenergetic, macronutrient-controlled, low-GI-starch diets. In a study of healthy pregnant women, a high-GI diet was associated with greater weight at term than was a nutrient-balanced, low-GI diet. In a study of diet and complications of type 1 diabetes, the GI of the overall diet was an independent predictor of waist circumference in men. These findings provide the scientific rationale to justify randomized, controlled, multicenter intervention studies comparing the effects of conventional and low-GI diets on weight control.

PMID: 12081852 [PubMed - indexed for MEDLINE]



Am J Clin Nutr. 2000 Aug;72(2):439-49. [Related Articles](#). [Links](#)

Comparison of high- and low-glycemic-index breakfast cereals with monounsaturated fat in the long-term dietary management of type 2 diabetes.

[Tsihlias EB](#), [Gibbs AL](#), [McBurney MI](#), [Wolever TM](#).

Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Canada.

BACKGROUND: Results of 6-wk studies suggest that high-carbohydrate diets are deleterious for people with type 2 diabetes. **OBJECTIVE:** Our objective was to see whether long-term replacement of dietary monounsaturated fatty acids (MUFAs) with carbohydrate from breakfast cereals with either a high or a low glycemic index (GI) affected blood glucose and lipids in subjects with type 2 diabetes. **DESIGN:** Subjects with type 2 diabetes (n = 91) were randomly assigned to receive approximately 10% of energy from a low-GI breakfast cereal, a high-GI cereal, or oil or margarine containing MUFA for 6 mo. Eating breakfast cereal was prohibited for subjects in the MUFA group. **RESULTS:** Seventy-two subjects completed the trial. The subjects who received cereals consumed approximately 10% more energy from carbohydrate than did the subjects in the MUFA group. Changes in glycated hemoglobin, body weight, and fasting cholesterol and triacylglycerol did not differ significantly among groups. HDL cholesterol increased by approximately 10% in the MUFA group compared with

subjects who consumed either high- or low-GI cereals ($P = 0.002$). The ratio of total to HDL cholesterol was higher in the subjects who consumed the high-GI cereal than in the MUFA group at 3 mo but not at 6 mo (diet x time interaction, $P = 0.041$). During 8-h metabolic profiles, mean plasma insulin was higher and mean free fatty acids were lower in the 2 cereal groups than in the MUFA group ($P < 0.05$). CONCLUSIONS: A 10% increase in carbohydrate intake associated with breakfast cereal consumption had no deleterious effects on glycemic control or blood lipids over 6 mo in subjects with type 2 diabetes. The increase in plasma insulin and the reduction in free fatty acids associated with higher carbohydrate intake may reduce the rate of progression of diabetes.

Publication Types:

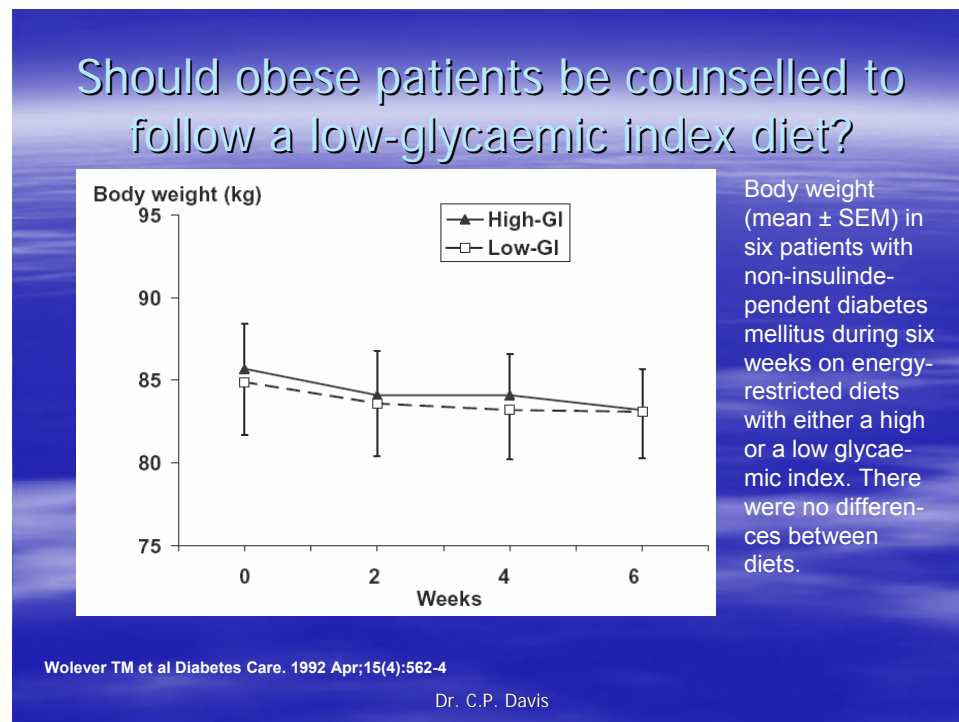
Clinical Trial

Comparative Study

Randomized Controlled Trial

Research Support, Non-U.S. Gov't

PMID: 10919939 [PubMed - indexed for MEDLINE]



Diabetes Care. 1992 Apr;15(4):562-4. [Related Articles](#), [Links](#)

Beneficial effect of low-glycemic index diet in overweight NIDDM subjects.

[Wolever TM](#), [Jenkins DJ](#), [Vuksan V](#), [Jenkins AL](#), [Wong GS](#), [Josse RG](#).

Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Ontario, Canada.

OBJECTIVE--To determine whether low-glycemic index (GI) diets have clinical utility in overweight patients with non-insulin-dependent diabetes mellitus (NIDDM). RESEARCH DESIGN AND METHODS--Six patients with NIDDM were studied on both high- and low-GI diets of 6-wk duration with metabolic diets with a randomized crossover design. Both diets

were of similar composition (57% carbohydrate, 23% fat, and 34 g/day dietary fiber), but the low-GI diet had a GI of 58 compared with 86 for the high-GI diet. RESULTS--Small and similar amounts of weight were lost on both diets: 2.5 kg on high-GI diet and 1.8 kg on low-GI diet. On the low-GI diet, the mean level of serum fructosamine, as an index of overall blood glucose control, was lower than on the high-GI diet by 8% (P less than 0.05), and total serum cholesterol was lower by 7% (P less than 0.01). CONCLUSIONS--In overweight patients with NIDDM, reducing diet GI improves overall blood glucose and lipid control.

Publication Types:

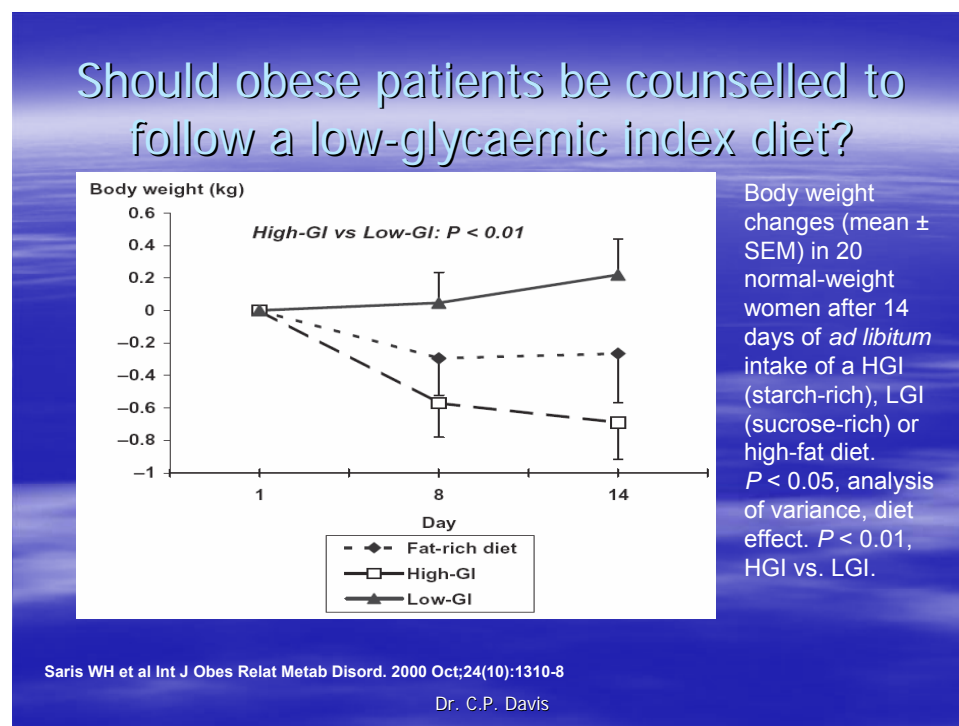
Clinical Trial

Comparative Study

Randomized Controlled Trial

Research Support, Non-U.S. Gov't

PMID: 1499480 [PubMed - indexed for MEDLINE]



Int J Obes Relat Metab Disord. 2000 Oct;24(10):1310-8. Links

Randomized controlled trial of changes in dietary carbohydrate/fat ratio and simple vs complex carbohydrates on body weight and blood lipids: the CARMEN study. The Carbohydrate Ratio Management in European National diets.

[Saris WH](#),

[Astrup A](#),

[Prentice AM](#),

[Zunft HJ](#),

[Formiguera X](#),

[Verboeket-van de Venne WP](#),

[Raben A](#),

[Poppitt SD](#),

[Seppelt B](#),

[Johnston S](#),

[Vasilaras TH](#),

Keogh GF.

Nutrition and Toxicology Research Institute Maastricht, Maastricht University, The Netherlands. W.Saris@HB.UNIMAAS.NL

OBJECTIVE: To investigate the long-term effects of changes in dietary carbohydrate/fat ratio and simple vs complex carbohydrates. **DESIGN:** Randomized controlled multicentre trial (CARMEN), in which subjects were allocated for 6 months either to a seasonal control group (no intervention) or to one of three experimental groups: a control diet group (dietary intervention typical of the average national intake); a low-fat high simple carbohydrate group; or a low-fat high complex carbohydrate group. **SUBJECTS:** Three hundred and ninety eight moderately obese adults. **MEASUREMENTS:** The change in body weight was the primary outcome; changes in body composition and blood lipids were secondary outcomes. **RESULTS:** Body weight loss in the low-fat high simple carbohydrate and low-fat high complex carbohydrate groups was 0.9 kg ($P < 0.05$) and 1.8 kg ($P < 0.001$), while the control diet and seasonal control groups gained weight (0.8 and 0.1 kg, NS). Fat mass changed by -1.3kg ($P < 0.01$), -1.8kg ($P < 0.001$) and +0.6kg (NS) in the low-fat high simple carbohydrate, low-fat high complex carbohydrate and control diet groups, respectively. Changes in blood lipids did not differ significantly between the dietary treatment groups. **CONCLUSION:** Our findings suggest that reduction of fat intake results in a modest but significant reduction in body weight and body fatness. The concomitant increase in either simple or complex carbohydrates did not indicate significant differences in weight change. No adverse effects on blood lipids were observed. These findings underline the importance of this dietary change and its potential impact on the public health implications of obesity.

PMID: 11093293 [PubMed - indexed for MEDLINE]

Should obese patients be counselled to follow a low-glycaemic index diet? NO!

- The data from short-term human intervention studies does not provide convincing evidence that low-GI meals have a more positive effect on satiety, hunger and food intake than high-GI meals
 - The summary of 31 studies which measured hunger and/or satiety shows that a low-GI test meal was associated with greater satiety or reduced hunger in 15 studies, whereas there was no difference in 16 other studies
- 13 isoenergetic long-term studies reported a greater weight loss on a low-GI diet in two studies and a greater weight loss on a high-GI diet in one study. In 10 studies, however, no differences were observed
- Data from five studies using energy restricted diets showed that a LGI diet decreased body weight in two studies, whereas there were no differences in the remaining three studies
 - The mean weight loss was somewhat larger on LGI (4.8 kg) than on HGI (3.3 kg) diets, which might indicate a possible benefit of LGI diets

Raben A Obes Rev. 2002 Nov;3(4):245-56

Dr. C.P. Davis

Obes Rev. 2002 Nov;3(4):245-56. [Links](#)

Comment in:

[Obes Rev. 2002 Nov;3\(4\):233.](#)

[Obes Rev. 2003 Feb;4\(1\):73-4.](#)

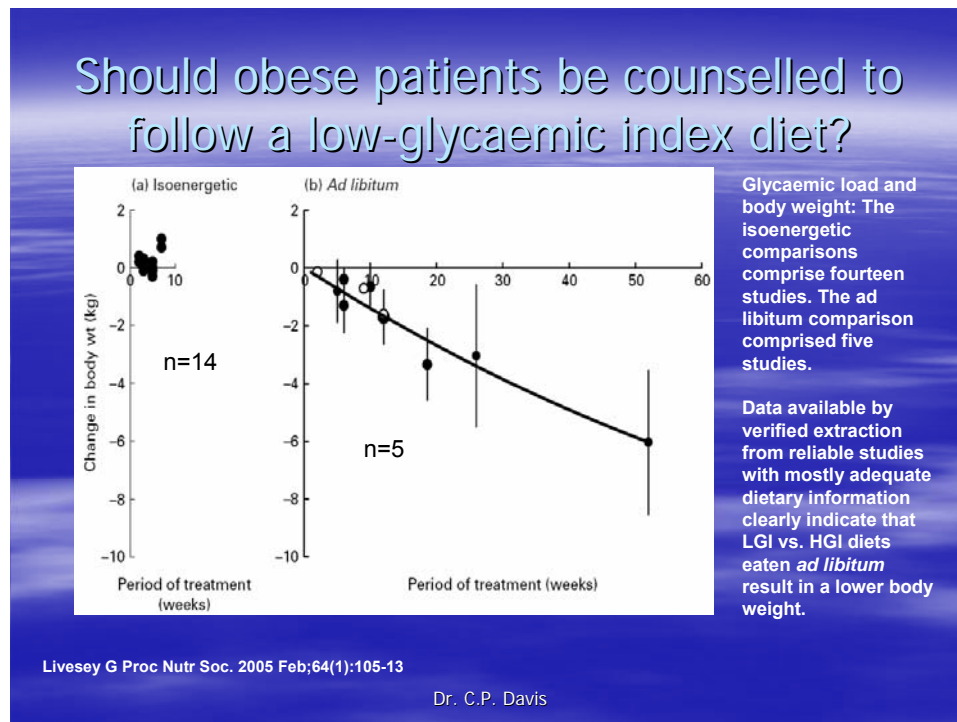
Should obese patients be counselled to follow a low-glycaemic index diet? No.

[Raben A.](#)

Research Department of Human Nutrition, Centre for Advanced Food Studies, The Royal Veterinary and Agricultural University, Frederiksberg, Denmark. ar@kvl.dk

In diabetes research the glycaemic index (GI) of carbohydrates has long been recognized and a low GI is recommended. The same is now often the case in lipid research. Recently, a new debate has arisen around whether a low-GI diet should also be advocated for appetite- and long-term body weight control. A systematic review was performed of published human intervention studies comparing the effects of high- and low-GI foods or diets on appetite, food intake, energy expenditure and body weight. In a total of 31 short-term studies (< 1 d), low-GI foods were associated with greater satiety or reduced hunger in 15 studies, whereas reduced satiety or no differences were seen in 16 other studies. Low-GI foods reduced ad libitum food intake in seven studies, but not in eight other studies. In 20 longer-term studies (< 6 months), a weight loss on a low-GI diet was seen in four and on a high-GI diet in two, with no difference recorded in 14. The average weight loss was 1.5 kg on a low-GI diet and 1.6 kg on a high-GI diet. To conclude, there is no evidence at present that low-GI foods are superior to high-GI foods in regard to long-term body weight control. However, the ideal long-term study where ad libitum intake and fluctuations in body weight are permitted, and the diets are similar in all aspects except GI, has not yet been performed.

PMID: 12458971 [PubMed - indexed for MEDLINE]



Proc Nutr Soc. 2005 Feb;64(1):105-13. [Links](#)

Low-glycaemic diets and health: implications for obesity.

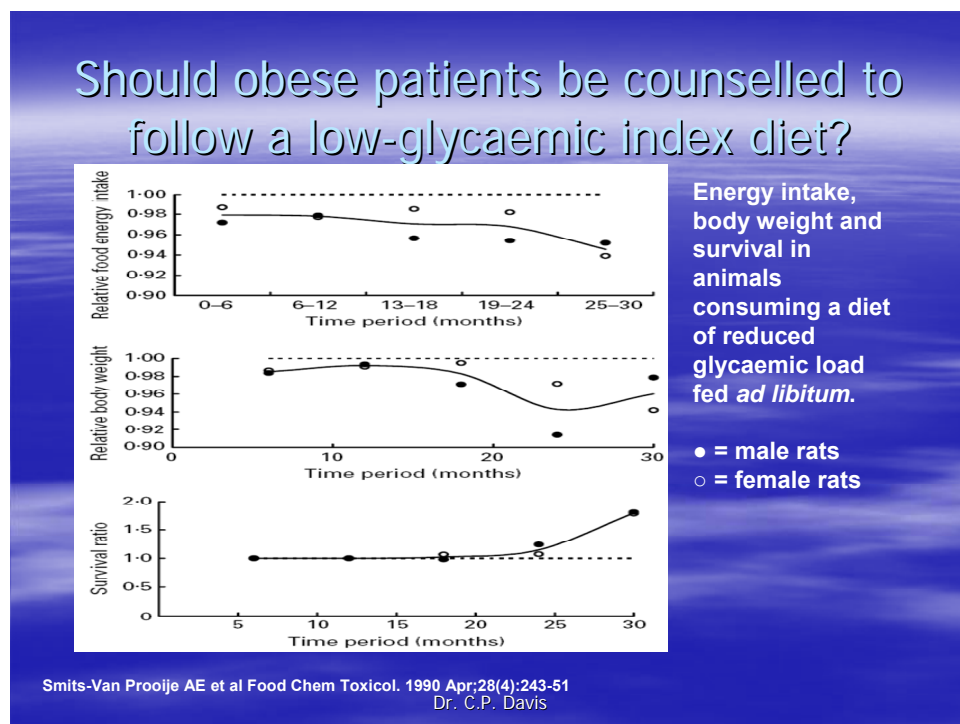
[Livesey G.](#)

Independent Nutrition Logic Ltd, Wymondham, Norfolk, UK. glivesey@inlogic.co.uk

The present review considers the background to terminology that relates foods, glycaemia and health, including 'available carbohydrate', 'glycaemic index' (GI), 'glycaemic glucose equivalent', 'glycaemic response index' and 'net carbohydrate', and concludes that central to each of these terms is 'glycaemic load' (GL). GL represents the acute increase in exposure of tissue to glucose determined by foods; it is expressed in ingested glucose equivalents (per 100 g fresh weight or per serving), and is regarded as independent of the state of glucose metabolism from normal to type 2 diabetes mellitus (T2DM). Ad libitum studies in

overweight or obese adults and children show that low-GL diets are associated with marked weight benefits, loss of adiposity and reduced food intake. Weight benefits appear on low-glycaemic v. high-glycaemic available carbohydrates, unavailable v. available carbohydrates and protein v. available carbohydrate. Energy intake immediately after lowering of meal GL via carbohydrate exchanges is apparent only after a threshold cumulative intake of >2000 MJ. Various epidemiological and interventional studies are discussed. A relationship between GL and the development of T2DM and CHD is evident. Studies that at first seem conflicting are actually consistent when data are overlaid, such that diets with a GL of >120 glucose equivalents/d would appear to be inadvisable. Whereas certain studies might place GI as being slightly stronger than GL in relation to T2DM risk, this situation appears to be associated with observations in a lower range of GL or when the range of GI is too narrow for accuracy; nevertheless, authors emphasise the importance of GL. Among the studies reviewed, GL offers a better or stronger explanation than GI in various observations including body weight, T2DM in nurses, CHD, plasma triacylglycerols, HDL-cholesterol, high-sensitivity C-reactive protein and protein glycation. Where information is available, the associations between risk factors and GL are either similar or stronger in the overweight or obese, as judged by BMI, and apply to both body weight and blood risk factors. The implications tend to favour a long-term benefit of reducing GL, for which further study is necessary to eliminate any possibility of publication bias and to establish results in clinical trials with overweight and obese patients.

PMID: 15877929 [PubMed - indexed for MEDLINE]



Food Chem Toxicol. 1990 Apr;28(4):243-51. Links

Chronic toxicity and carcinogenicity study of isomalt in rats and mice.

[Smits-Van Prooijje AE,](#)

[De Groot AP,](#)

[Dreef-Van der Meulen HC,](#)

[Sinkeldam EJ.](#)

Department of Biological Toxicology, TNO-CIVO Toxicology and Nutrition Institute, Zeist, The Netherlands.

The chronic toxicity and possible carcinogenicity of the sugar replacer isomalt was studied in Wistar rats and Swiss mice. Groups of 50 animals of each sex were fed 0, 2.5, 5 or 10% isomalt in the diet for nearly 2.5 yr (rats) or 2 yr (mice). Control groups received either basal diet with 10% maize starch or basal diet with 10% sucrose. Additional groups of ten rats/sex were fed the same diets and were killed after 1 yr. Isomalt and sucrose were included in the diet at the expense of maize starch. Administration of isomalt was started, in rats, in utero, and in mice, at weaning age. Feeding isomalt did not affect the appearance or behaviour of rats or mice, nor did it cause diarrhoea. Mortality rate was unaffected. Body weights of rats and mice fed 10% isomalt were generally slightly lower than those of controls. Periodic examinations of rats for haematological criteria, clinical chemistry of the blood, urine composition and kidney function did not reveal any changes of toxicological significance. Periodic haematological examinations of mice were likewise negative. Caecal enlargement was observed in rats and mice of the high-dose group, but the microscopic structure of the caecal wall was unaffected. An increased number of treated male and female rats showed hyperplasia of the urothelium in the renal pelvis accompanied by mineralization, whereas the number of females showing corticomedullary mineralization was decreased in the treated groups. The incidence, type or location of neoplasia provided no evidence of a carcinogenic potential of isomalt. Feeding 10% sucrose did not induce significant differences compared with the controls fed 10% maize starch, whereas isomalt at levels of up to 10% produced some of the changes that are common to rats fed high levels of poorly digestible carbohydrates.

PMID: 2358250 [PubMed - indexed for MEDLINE]

Should obese patients be counselled to follow a low-glycaemic index diet? YES!

- Weight loss on energy-restricted, reduced-fat diets may be increased when such diets are modified to lower GI
- When energy intake is not restricted, low GI and/or glycaemic load diets may produce greater weight loss than conventional, low-fat diets
- A low GI diet may, in addition, modulate the rate of weight gain during physiological states of increased nutrient storage, such as pregnancy
 - Lower intra-pregnancy weight gain with a LGI diet (11.8 vs. 19.7 kg, $P < 0.01$)
- Reduction in GI or glycaemic load would be predicted to have beneficial effects on rates of lipid oxidation and preservation of lean body tissue

Pawlak DB *Obes Rev.* 2002 Nov;3(4):235-43
Clapp JI *Arch Gynecol Obstet* 1997; 261: 101-107

Dr. C.P. Davis

Obes Rev. 2002 Nov;3(4):235-43. [Links](#)

Comment in:

[Obes Rev.](#) 2002 Nov;3(4):233.

Should obese patients be counselled to follow a low-glycaemic index diet? Yes.

[Pawlak DB](#),
[Ebbeling CB](#),
[Ludwig DS](#).

Department of Medicine, Children's Hospital, Boston, MA 02115, USA.

A reduction in dietary fat has been widely advocated for the prevention and treatment of obesity and related complications. However, the efficacy of low-fat diets has been questioned in recent years. One potential adverse effect of reduced dietary fat is a compensatory increase in the consumption of high glycaemic index (GI) carbohydrate, principally refined starchy foods and concentrated sugar. Such foods can be rapidly digested or transformed into glucose, causing a large increase in post-prandial blood glucose and insulin. Short-term feeding studies have generally found an inverse association between GI and satiety. Medium-term clinical trials have found less weight loss on high GI or high glycaemic load diets compared to low GI or low glycaemic load diets. Epidemiological analyses link GI to multiple cardiovascular disease risk factors and to the development of cardiovascular disease and type 2 diabetes. Physiologically orientated studies in humans and animal models provide support for a role of GI in disease prevention and treatment. This review examines the mechanisms underlying the potential benefits of a low GI diet, and whether such diets should be recommended in the clinical setting.

PMID: 12458970 [PubMed - indexed for MEDLINE]

Should obese patients be counselled to follow a low-glycaemic index diet? YES!

- LGI diets might decrease risk for type 2 diabetes, independent of weight change, by reducing demand on the pancreatic β cell in the postprandial period and also by decreasing insulin resistance
 - lower average 24-hour blood glucose levels
 - lower average 24-hour insulin levels
 - lower C-peptide excretion
- LGI diets lead to lower glycated hemoglobin (HbA1c) concentrations in nondiabetic and diabetic individuals
 - An increase of 1% in HbA(1c) is associated with a 28% ($P<0.002$) increase in risk of death independent of age, blood pressure, serum cholesterol, body mass index, and cigarette smoking habit

Jenkins DJ, et al. Am J Clin Nutr. 1987 Dec;46(6):968-75
Miller JC Am J Clin Nutr. 1994 Mar;59(3 Suppl):747S-752S
Livesey G Nutr Res Rev. 2003 38:117-121
Khaw KT et al BMJ. 2001 Jan 6;322(7277):15-8

Dr. C.P. Davis

Am J Clin Nutr. 1987 Dec;46(6):968-75. Links
Metabolic effects of a low-glycemic-index diet.

[Jenkins DJ,](#)
[Wolever TM,](#)
[Collier GR,](#)
[Ocana A,](#)
[Rao AV,](#)
[Buckley G,](#)
[Lam Y,](#)
[Mayer A,](#)
[Thompson LU.](#)

Department of Nutritional Sciences, Faculty of Medicine, University of Toronto, Ontario, Canada.

Six healthy male volunteers underwent 2-wk metabolically controlled high-glycemic-index (GI) and low-GI diets in random order. Over the low-GI diet significant reductions were seen in serum fructosamine (7.0 +/- 1.0%, p less than 0.01), 12-h blood glucose profile (37 +/- 7%, p less than 0.01), and total serum cholesterol (15 +/- 3%, p less than 0.01). As a measure of insulin secretion, 24-h urinary C-peptide levels were 32 +/- 10% lower (p less than 0.05) after the low-GI than after the high-GI diet. Lower C-peptide levels were maintained after a standard carbohydrate challenge after the low-GI diet despite higher blood glucose levels. Differences in blood glucose were not seen after a 5-g intravenous glucose challenge. These results are of interest with respect to the effect that prolonged postprandial reductions in nutrient fluxes and insulin secretion may have on carbohydrate and lipid metabolism and renal function.

PMID: 2825505 [PubMed - indexed for MEDLINE]

Am J Clin Nutr. 1994 Mar;59(3 Suppl):747S-752S. Links

Importance of glycemic index in diabetes.

[Miller JC.](#)

Department of Biochemistry, University of Sydney, New South Wales, Australia.

To date there are 11 medium to long-term studies that have specifically used the glycemic index (GI) approach to determine the clinical gains in diabetes or lipid management. All but one study produced positive findings. On average, low-GI diets reduced glycosylated hemoglobin by 9%, fructosamine by 8%, urinary C-peptide by 20%, and day-long blood glucose by 16%. Cholesterol was reduced by an average of 6% and triglycerides by 9%. These are modest improvements but so too were the changes to the diet. Unlike high-fiber diets, low-GI diets are "user friendly." As part of studies on the GI of foods, we determined the glycemic and insulin responses to 44 foods containing simple sugars. Their mean (+/- SE) GI was 62 +/- 14, which compares favorably with bread (GI = 73, glucose = 100). There was often no difference in the GI between the sweetened and unsweetened product. The time has come to reassess the value of GI in planning meals for diabetics.

PMID: 8116560 [PubMed - indexed for MEDLINE]

Stroke. 2007 Feb;38(2):271-5. Epub 2007 Jan 4. Links

Glycated hemoglobin and risk of stroke in people without known diabetes in the European Prospective Investigation into Cancer (EPIC)-Norfolk prospective population study: a threshold relationship?

[Myint PK.](#)

[Sinha S.](#)

[Wareham NJ.](#)

[Bingham SA.](#)

[Luben RN.](#)

[Welch AA.](#)

[Khaw KT.](#)

Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK.

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BACKGROUND AND PURPOSE: Diabetes is a well-recognized risk factor for cardiovascular diseases. Evidence suggests a linear relationship between blood glucose and myocardial infarction, even at blood glucose concentrations below the threshold for diabetes. The relationship between blood glucose concentration and stroke in people without established diabetes has been studied less extensively. **METHODS:** We examined the prospective relationship between usual blood glucose level measured by glycohemoglobin (HbA(1c)) concentrations and incident stroke risk in a general population without diabetes

and stroke at baseline assessment in the European Prospective Investigation Into Cancer (EPIC)-Norfolk. RESULTS: A total of 10,489 men and women aged 40 to 79 years at baseline were followed up (mean=8.5 years). Mean age, systolic and diastolic blood pressure, body mass index, total cholesterol, triglycerides, and proportion of current smokers increased and mean high-density lipoprotein cholesterol decreased with increasing HbA(1c) concentrations. There were 164 incident strokes identified over 88 652 person-years. After adjustment for age, sex, and cardiovascular risk factors, the relative risks (95% CI) for stroke for participants with HbA(1c) concentrations 5% to 5.4%, 5.5% to 6.9%, and $\geq 7\%$ were 0.78 (0.50 to 1.22), 0.83 (0.54 to 1.27), and 2.83 (1.40 to 5.74), respectively, compared with those with HbA(1c) $< 5\%$. CONCLUSIONS: In contrast to the continuous linear relationship observed between blood glucose level and coronary heart disease risk, the association between blood glucose level and stroke risk appears to be more consistent with a threshold relationship. These observations may give insights into the differing pathogenesis of different vascular diseases.

PMID: 17204684 [PubMed - indexed for MEDLINE]

BMJ. 2001 Jan 6;322(7277):15-8. [Links](#)

Comment in:

[BMJ. 2001 Apr 21;322\(7292\):996-7.](#)

[BMJ. 2001 Apr 21;322\(7292\):996; author reply 996-7.](#)

[BMJ. 2001 Apr 21;322\(7292\):997.](#)

[BMJ. 2001 Jan 6;322\(7277\):5-6.](#)

Glycated haemoglobin, diabetes, and mortality in men in Norfolk cohort of european prospective investigation of cancer and nutrition (EPIC-Norfolk).

[Khaw KT,](#)

[Wareham N,](#)

[Luben R,](#)

[Bingham S,](#)

[Oakes S,](#)

[Welch A,](#)

[Day N.](#)

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OBJECTIVE: To examine the value of glycated haemoglobin (HbA(1c)) concentration, a marker of blood glucose concentration, as a predictor of death from cardiovascular and all causes in men. DESIGN: Prospective population study. SETTING: Norfolk cohort of

European Prospective Investigation into Cancer and Nutrition (EPIC-Norfolk). SUBJECTS: 4662 men aged 45-79 years who had had glycated haemoglobin measured at the baseline

survey in 1995-7 who were followed up to December 1999. MAIN OUTCOME

MEASURES: Mortality from all causes, cardiovascular disease, ischaemic heart disease, and other causes. RESULTS: Men with known diabetes had increased mortality from all causes,

cardiovascular disease, and ischaemic disease (relative risks 2.2, 3.3, and 4.2, respectively, $P < 0.001$ independent of age and other risk factors) compared with men without known

diabetes. The increased risk of death among men with diabetes was largely explained by HbA(1c) concentration. HbA(1c) was continuously related to subsequent all cause,

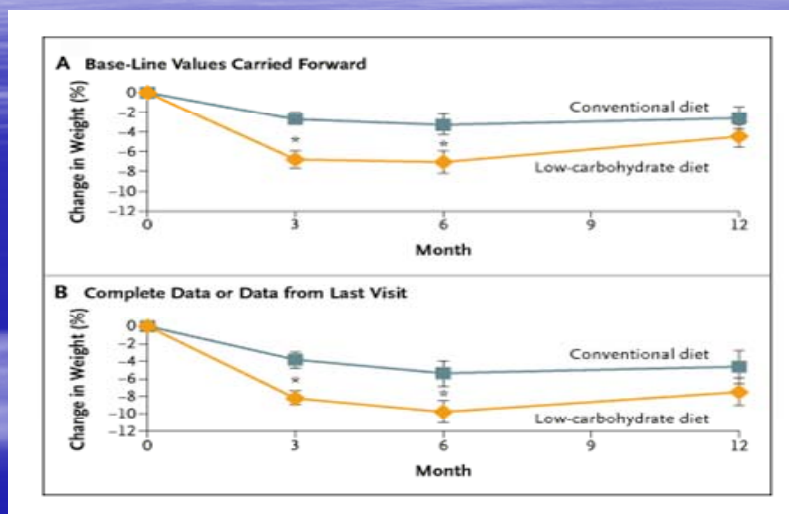
cardiovascular, and ischaemic heart disease mortality through the whole population distribution, with lowest rates in those with HbA(1c) concentrations below 5%. An increase of

1% in HbA(1c) was associated with a 28% ($P < 0.002$) increase in risk of death independent of age, blood pressure, serum cholesterol, body mass index, and cigarette smoking habit; this

effect remained (relative risk 1.46, $P = 0.05$ adjusted for age and risk factors) after men with

known diabetes, a HbA(1c) concentration $\geq 7\%$, or history of myocardial infarction or stroke were excluded. 18% of the population excess mortality risk associated with a HbA(1c) concentration $\geq 5\%$ occurred in men with diabetes, but 82% occurred in men with concentrations of 5%-6.9% (the majority of the population). CONCLUSIONS: Glycated haemoglobin concentration seems to explain most of the excess mortality risk of diabetes in men and to be a continuous risk factor through the whole population distribution. Preventive efforts need to consider not just those with established diabetes but whether it is possible to reduce the population distribution of HbA(1c) through behavioural means.
PMID: 11141143 [PubMed - indexed for MEDLINE]

Comparison of Weight Loss between a Conventional and a low-COH Diet



Foster GD et al. N Engl J Med 2003 22;348(21):2082-90 Dr. C.P. Davis

N Engl J Med. 2003 May 22;348(21):2082-90. Links

Comment in:

[N Engl J Med. 2003 May 22;348\(21\):2057-8.](#)

[N Engl J Med. 2003 May 22;348\(21\):2136-7.](#)

[N Engl J Med. 2003 Sep 4;349\(10\):1000-2; author reply 1000-2.](#)

[N Engl J Med. 2003 Sep 4;349\(10\):1000-2; author reply 1000-2.](#)

A randomized trial of a low-carbohydrate diet for obesity.

[Foster GD](#),

[Wyatt HR](#),

[Hill JO](#),

[McGuckin BG](#),

[Brill C](#),

[Mohammed BS](#),

[Szapary PO](#),

[Rader DJ](#),

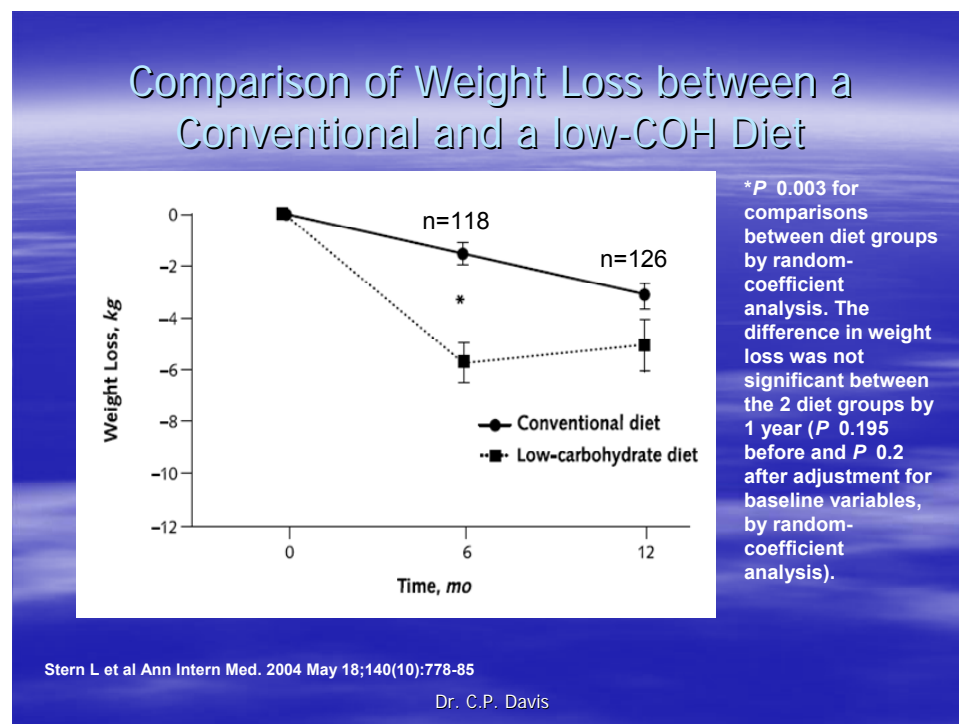
[Edman JS](#),

[Klein S](#).

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BACKGROUND: Despite the popularity of the low-carbohydrate, high-protein, high-fat (Atkins) diet, no randomized, controlled trials have evaluated its efficacy. **METHODS:** We conducted a one-year, multicenter, controlled trial involving 63 obese men and women who were randomly assigned to either a low-carbohydrate, high-protein, high-fat diet or a low-calorie, high-carbohydrate, low-fat (conventional) diet. Professional contact was minimal to replicate the approach used by most dieters. **RESULTS:** Subjects on the low-carbohydrate diet had lost more weight than subjects on the conventional diet at 3 months (mean [\pm SD], -6.8 \pm 5.0 vs. -2.7 \pm 3.7 percent of body weight; $P=0.001$) and 6 months (-7.0 \pm 6.5 vs. -3.2 \pm 5.6 percent of body weight, $P=0.02$), but the difference at 12 months was not significant (-4.4 \pm 6.7 vs. -2.5 \pm 6.3 percent of body weight, $P=0.26$). After three months, no significant differences were found between the groups in total or low-density lipoprotein cholesterol concentrations. The increase in high-density lipoprotein cholesterol concentrations and the decrease in triglyceride concentrations were greater among subjects on the low-carbohydrate diet than among those on the conventional diet throughout most of the study. Both diets significantly decreased diastolic blood pressure and the insulin response to an oral glucose load. **CONCLUSIONS:** The low-carbohydrate diet produced a greater weight loss (absolute difference, approximately 4 percent) than did the conventional diet for the first six months, but the differences were not significant at one year. The low-carbohydrate diet was associated with a greater improvement in some risk factors for coronary heart disease. Adherence was poor and attrition was high in both groups. Longer and larger studies are required to determine the long-term safety and efficacy of low-carbohydrate, high-protein, high-fat diets. Copyright 2003 Massachusetts Medical Society PMID: 12761365 [PubMed - indexed for MEDLINE]



Ann Intern Med. 2004 May 18;140(10):778-85. Links
Comment in:

[Ann Intern Med. 2004 May 18;140\(10\):836-7.](#)

[Ann Intern Med. 2004 May 18;140\(10\):I27.](#)

[Ann Intern Med. 2004 Nov 2;141\(9\):738; author reply 738-9.](#)

The effects of low-carbohydrate versus conventional weight loss diets in severely obese adults: one-year follow-up of a randomized trial.

[Stern L,](#)

[Iqbal N,](#)

[Seshadri P,](#)

[Chicano KL,](#)

[Daily DA,](#)

[McGrory J,](#)

[Williams M,](#)

[Gracely EJ,](#)

[Samaha FF.](#)

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BACKGROUND: A previous paper reported the 6-month comparison of weight loss and metabolic changes in obese adults randomly assigned to either a low-carbohydrate diet or a conventional weight loss diet. **OBJECTIVE:** To review the 1-year outcomes between these diets. **DESIGN:** Randomized trial. **SETTING:** Philadelphia Veterans Affairs Medical Center. **PARTICIPANTS:** 132 obese adults with a body mass index of 35 kg/m² or greater; 83% had diabetes or the metabolic syndrome. **INTERVENTION:** Participants received counseling to either restrict carbohydrate intake to <30 g per day (low-carbohydrate diet) or to restrict caloric intake by 500 calories per day with <30% of calories from fat (conventional diet). **MEASUREMENTS:** Changes in weight, lipid levels, glycemic control, and insulin sensitivity. **RESULTS:** By 1 year, mean (+/-SD) weight change for persons on the low-carbohydrate diet was -5.1 +/- 8.7 kg compared with -3.1 +/- 8.4 kg for persons on the conventional diet. Differences between groups were not significant (-1.9 kg [95% CI, -4.9 to 1.0 kg]; P = 0.20). For persons on the low-carbohydrate diet, triglyceride levels decreased more (P = 0.044) and high-density lipoprotein cholesterol levels decreased less (P = 0.025). As seen in the small group of persons with diabetes (n = 54) and after adjustment for covariates, hemoglobin A1c levels improved more for persons on the low-carbohydrate diet. These more favorable metabolic responses to a low-carbohydrate diet remained significant after adjustment for weight loss differences. Changes in other lipids or insulin sensitivity did not differ between groups. **LIMITATIONS:** These findings are limited by a high dropout rate (34%) and by suboptimal dietary adherence of the enrolled persons. **CONCLUSION:** Participants on a low-carbohydrate diet had more favorable overall outcomes at 1 year than did those on a conventional diet. Weight loss was similar between groups, but effects on atherogenic dyslipidemia and glycemic control were still more favorable with a low-carbohydrate diet after adjustment for differences in weight loss.

PMID: 15148064 [PubMed - indexed for MEDLINE]

Comparison of different diets with respect to compliance

Mean Self-reported Dietary Adherence Scores of All 4 Diet Groups, According to Study Month



Dansinger ML et al. JAMA. 2005 Jan 5;293(1):43-53

Dr. C.P. Davis

JAMA. 2005 Jan 5;293(1):43-53. [Related Articles](#), [Links](#)

Comment in:

[J Fam Pract. 2005 Apr;54\(4\):306.](#)

[JAMA. 2005 Apr 6;293\(13\):1589-90; author reply 1590-1.](#)

[JAMA. 2005 Apr 6;293\(13\):1590; author reply 1590-1.](#)

[JAMA. 2005 Jan 5;293\(1\):96-7.](#)

Comparison of the Atkins, Ornish, Weight Watchers, and Zone diets for weight loss and heart disease risk reduction: a randomized trial.

[Dansinger ML](#), [Gleason JA](#), [Griffith JL](#), [Selker HP](#), [Schaefer EJ](#).

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CONTEXT: The scarcity of data addressing the health effects of popular diets is an important public health concern, especially since patients and physicians are interested in using popular diets as individualized eating strategies for disease prevention. **OBJECTIVE:** To assess adherence rates and the effectiveness of 4 popular diets (Atkins, Zone, Weight Watchers, and Ornish) for weight loss and cardiac risk factor reduction. **DESIGN, SETTING, AND PARTICIPANTS:** A single-center randomized trial at an academic medical center in Boston, Mass, of overweight or obese (body mass index: mean, 35; range, 27-42) adults aged 22 to 72 years with known hypertension, dyslipidemia, or fasting hyperglycemia. Participants were enrolled starting July 18, 2000, and randomized to 4 popular diet groups until January 24, 2002. **INTERVENTION:** A total of 160 participants were randomly assigned to either Atkins (carbohydrate restriction, n=40), Zone (macronutrient balance, n=40), Weight Watchers (calorie restriction, n=40), or Ornish (fat restriction, n=40) diet groups. After 2 months of maximum effort, participants selected their own levels of dietary adherence. **MAIN OUTCOME MEASURES:** One-year changes in baseline weight and cardiac risk factors, and self-selected dietary adherence rates per self-report. **RESULTS:** Assuming no change from

baseline for participants who discontinued the study, mean (SD) weight loss at 1 year was 2.1 (4.8) kg for Atkins (21 [53%] of 40 participants completed, $P = .009$), 3.2 (6.0) kg for Zone (26 [65%] of 40 completed, $P = .002$), 3.0 (4.9) kg for Weight Watchers (26 [65%] of 40 completed, $P < .001$), and 3.3 (7.3) kg for Ornish (20 [50%] of 40 completed, $P = .007$). Greater effects were observed in study completers. Each diet significantly reduced the low-density lipoprotein/high-density lipoprotein (HDL) cholesterol ratio by approximately 10% (all $P < .05$), with no significant effects on blood pressure or glucose at 1 year. Amount of weight loss was associated with self-reported dietary adherence level ($r = 0.60$; $P < .001$) but not with diet type ($r = 0.07$; $P = .40$). For each diet, decreasing levels of total/HDL cholesterol, C-reactive protein, and insulin were significantly associated with weight loss (mean $r = 0.36, 0.37$, and 0.39 , respectively) with no significant difference between diets ($P = .48, P = .57, P = .31$, respectively). CONCLUSIONS: Each popular diet modestly reduced body weight and several cardiac risk factors at 1 year. Overall dietary adherence rates were low, although increased adherence was associated with greater weight loss and cardiac risk factor reductions for each diet group.

Publication Types:

Clinical Trial

Randomized Controlled Trial

PMID: 15632335 [PubMed - indexed for MEDLINE]